```
=> file biosis caba caplus embase japio lifesci medline scisearch
=> e lubitz werner/au
E1            1     LUBITZ W D/AU
E2            1     LUBITZ W J/AU
E3          389 --> LUBITZ WERNER/AU
E4            1     LUBITZ WERNER PROF/AU
E5            1     LUBITZ WILLIAM/AU
E6            2     LUBITZ WILLIAM DAVID/AU
E7            1     LUBITZ WOLFANG/AU
E8          372     LUBITZ WOLFGANG/AU
E9            1     LUBITZKI LOTHAR/AU
E10           1     LUBITZOMERO C/AU
E11           7     LUBITZSCH PETER/AU
E12           1     LUBITZSCH WOLFGANG/AU

=> s e1-e4 and ghost?
L1          152 ("LUBITZ W D"/AU OR "LUBITZ W J"/AU OR "LUBITZ WERNER"/AU OR
                "LUBITZ WERNER PROF"/AU) AND GHOST?

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2           54 DUP REM L1 (98 DUPLICATES REMOVED)

=> d l2 bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 54 ANSWERS - CONTINUE? Y/(N):y

L2   ANSWER 1 OF 54  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2009:140362  CAPLUS <<LOGINID::20090617>>
DN   150:176492
TI   Virus-modified bacterial   ***ghosts***   for gene therapy and
     nanotechnology elements
IN     ***Lubitz, Werner***
PA   Austria
SO   PCT Int. Appl., 20pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2009015852        A1    20090205    WO 2008-EP6207         20080728
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
             CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
             IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI EP 2007-14799        A     20070727
AB   The invention relates to virus-modified bacteria   ***ghosts***   and the
     use thereof, for example, as carrier and targeting vehicles for active
     ingredients.
```

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Virus-modified bacterial ***ghosts*** for gene therapy and nanotechnology elements

IN ***Lubitz, Werner***

AB The invention relates to virus-modified bacteria ***ghosts*** and the use thereof, for example, as carrier and targeting vehicles for active ingredients.

ST virus bacterial ***ghost*** bacteriophage peptide DNA drug delivery nanotechnol

IT Bacteriophage
(-modified bacterial ***ghost*** ; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Vaccines
(DNA; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Caudovirales
(Styloviridae; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Bacteriophage
(T; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Cell envelope
(bacterial ***ghost*** ; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Nucleic acids
Peptides, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterologous, phage-contg.; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix for bacterial ***ghosts*** ; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Immobilization, molecular or cellular
(of active substances in bacterial ***ghosts*** ; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Drug delivery systems
(targeted; virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

IT Coliphage .phi.X174
Corticoviridae
Escherichia coli
Filamentous bacteriophage
Gene therapy
Inoviridae
Lambda-like phages
Leviviridae
Microviridae
Myoviridae
Nanotechnology
Plasmaviridae
Podoviridae
Tectiviridae
(virus-modified bacterial ***ghosts*** for gene therapy and

nanotechnol. elements)
IT Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(virus-modified bacterial ***ghosts*** for gene therapy and nanotechnol. elements)

L2 ANSWER 2 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2008:583275 BIOSIS <<LOGINID::20090617>>
DN PREV200800583274
TI Nucleic acid free ***ghost*** preparations.
AU ***Lubitz, Werner*** [Inventor]; Anonymous; Haidinger, Wolfgang [Inventor]
CS Vienna, Austria
ASSIGNEE: Werner Lubitz
PI US 07399476 20080715
SO Official Gazette of the United States Patent and Trademark Office Patents, (JUL 15 2008)
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 22 Oct 2008
Last Updated on STN: 22 Oct 2008
AB The invention relates to preparations of bacterial ***ghosts*** which are substantially free of living bacterial cells and/or nucleic acids and their use in pharmaceutical preparations.
TI Nucleic acid free ***ghost*** preparations.
AU ***Lubitz, Werner*** [Inventor]; Anonymous; Haidinger, Wolfgang [Inventor]
AB The invention relates to preparations of bacterial ***ghosts*** which are substantially free of living bacterial cells and/or nucleic acids and their use in pharmaceutical preparations.
IT Major Concepts
Pharmacology
IT Chemicals & Biochemicals
nucleic acid free bacterial ***ghost*** preparation: antibacterial-drug, antiinfective-drug

L2 ANSWER 3 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 1
AN 2009:123003 BIOSIS <<LOGINID::20090617>>
DN PREV200900123003
TI Bacterial ***ghosts*** as a delivery system for zona pellucida-2 fertility control vaccines for brushtail possums (Trichosurus vulpecula).
AU Walcher, Petra; Cui, Xianlan; Arrow, Jane A.; Scobie, Susie; Molinia, Frank C.; Cowan, Phil E.; ***Lubitz, Werner*** ; Duckworth, Janine A. [Reprint Author]
CS Landcare Res, POB 40, Lincoln 7640, New Zealand
duckworthj@landcareresearch.co.nz
SO Vaccine, (DEC 9 2008) Vol. 26, No. 52, pp. 6832-6838.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 11 Feb 2009
Last Updated on STN: 11 Feb 2009
AB The introduced brushtail possum is a serious pest in New Zealand and there is much interest in the development of an immunocontraceptive vaccine for

population control. Immunisation of female possums against recombinant possum zona pellucida protein-2 (ZP2) is known to reduce embryo production by 72-75% but successful development of fertility control will depend on a delivery system that is effective Bacterial ***ghost*** vaccine technology is a promising system to formulate a non-living vaccine for for field use. bait or aerosol delivery. The N-terminal (amino acid residues 41-316, ZP2N) and C-terminal (amino acid residues 308-636, ZP2C) regions of possum ZP2 were fused to maltose-binding protein and expressed in the periplasmic space of Escherichia coli NM522 bacterial ***ghosts*** . Female possums (n = 20 per treatment group) were immunised with 20 mg of either plain ***ghosts*** , ZP2N ***ghosts*** , or ZP2C ***ghosts*** in phosphate-buffered saline applied to the nostrils and eyes (nasal/conjunctival mucosa) at weeks 0, 2 and 4. Effects of immunisation on fertility were assessed following superovulation and artificial insemination. Both constructs evoked humoral (antibody) and cell-mediated immune responses in possums and significantly fewer eggs were fertilised in females immunised against ZP2C ***ghosts*** . Results in this study indicate that bacterial ***ghosts*** containing possum ZP antigens can reduce possum fertility when delivered by mucosal immunisation and offer a promising delivery system for fertility control of wild possum populations. (C) 2008 Elsevier Ltd. All rights reserved.

TI Bacterial ***ghosts*** as a delivery system for zona pellucida-2 fertility control vaccines for brushtail possums (Trichosurus vulpecula).

AU Walcher, Petra; Cui, Xianlan; Arrow, Jane A.; Scobie, Susie; Molinia, Frank C.; Cowan, Phil E.; ***Lubitz, Werner*** ; Duckworth, Janine A. [Reprint Author]

AB. . . embryo production by 72-75% but successful development of fertility control will depend on a delivery system that is effective Bacterial ***ghost*** vaccine technology is a promising system to formulate a non-living vaccine for for field use. bait or aerosol delivery. The. . . regions of possum ZP2 were fused to maltose-binding protein and expressed in the periplasmic space of Escherichia coli NM522 bacterial ***ghosts*** . Female possums (n = 20 per treatment group) were immunised with 20 mg of either plain ***ghosts*** , ZP2N ***ghosts*** , or ZP2C ***ghosts*** in phosphate-buffered saline applied to the nostrils and eyes (nasal/conjunctival mucosa) at weeks 0, 2 and 4. Effects of immunisation. . . evoked humoral (antibody) and cell-mediated immune responses in possums and significantly fewer eggs were fertilised in females immunised against ZP2C ***ghosts*** . Results in this study indicate that bacterial ***ghosts*** containing possum ZP antigens can reduce possum fertility when delivered by mucosal immunisation and offer a promising delivery system for. . .

IT Methods & Equipment
bacterial ***ghost*** : drug delivery device

IT Miscellaneous Descriptors
immune response

L2 ANSWER 4 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 2

AN 2008:368954 BIOSIS <<LOGINID::20090617>>

DN PREV200800368953

TI Dendrosomes as novel gene porters-III.

AU Sadeghizadeh, Majid; Ranjbar, Bijan; Damaghi, Mehdi; Khaki, Leila; Sarbolouki, Mohammad N. [Reprint Author]; Najafi, Farhood; Parsaee, Simak; Ziaee, Abed-Ali; Massumi, Mohammad; ***Lubitz, Werner*** ; Kudela, Paul; Paukner, Susan; Karami, Ali

CS Univ Tehran, Inst Biochem and Biophys, POB 13145-1384, Tehran, Iran

sarbol@ibb.ut.ac.ir
SO Journal of Chemical Technology and Biotechnology, (JUN 2008) Vol. 83, No. 6, pp. 912-920.
CODEN: JCTBED. ISSN: 0268-2575.
DT Article
LA English
ED Entered STN: 2 Jul 2008
Last Updated on STN: 27 Aug 2008
AB BACKGROUND: It was previously reported that dendrosomes, i.e. neutral, biodegradable, covalent or self-assembled, hyperbranched, spheroidal nano-particles with a size ranging from 15 to 100 nm, provide a convenient and efficient means of gene delivery into various kinds of cells such as human hepatoma and kidney cells as well as animal models.RESULTS: New studies via circular dichroism show that hydrophilic and amphipathic dendrosomes either do not affect the DNA structure or moderately transform it from B- to A-conformation. Gene delivery into human liver, kidney, and endothelial cells as well as other animal cells like Bowes, U-937, Raw, CCRF-CEM, MOLT-4, K562, Huh-7 and VERO reveal that the genes are efficiently expressed and in comparison with other gene porters like Lipofectin or bacterial ***ghosts*** , do quite well. It is also shown that dendrosomes are able to deliver genes into cells like endothelials that are usually hard to transfect. Cell culture experiments as well as intraperitoneal/intradermal injections of dendrosomes into mice establish their nontoxicity (up to 2.5 mg kg(-1) of animal weight in the latter case). Studies on immunization of BALB/c mice using conventional adjuvants such as aluminium phosphate, C(p)G motif and one of the dendrosomes, indicate that the latter leads to the mildest initial response development while exceeding them afterwards.CONCLUSION: CD studies reveal that, owing to the neutrality of dendrosomes, formation of Den/DNA complexes is accompanied by slight structural modifications of DNA cell culture, and animal studies reveal that dendrosomes are inert, non-toxic and highly efficient gene porters that perform at extremely low doses. In comparison with bacterial ***ghosts*** and some common porters, they are efficient in delivery of genes into animals and a variety of cells including those that are usually hard to transfect. (c) 2008 Society of Chemical Industry.
AU. . . Majid; Ranjbar, Bijan; Damaghi, Mehdi; Khaki, Leila; Sarbolouki, Mohammad N. [Reprint Author]; Najafi, Farhood; Parsaee, Simak; Ziaee, Abed-Ali; Massumi, Mohammad; ***Lubitz, Werner*** ; Kudela, Paul; Paukner, Susan; Karami, Ali
AB. . . and VERO reveal that the genes are efficiently expressed and in comparison with other gene porters like Lipofectin or bacterial ***ghosts*** , do quite well. It is also shown that dendrosomes are able to deliver genes into cells like endothelials that are. . . that dendrosomes are inert, non-toxic and highly efficient gene porters that perform at extremely low doses. In comparison with bacterial ***ghosts*** and some common porters, they are efficient in delivery of genes into animals and a variety of cells including those. . .

L2 ANSWER 5 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 3
AN 2008:525668 BIOSIS <<LOGINID::20090617>>
DN PREV200800525667
TI Development of a Chlamydia trachomatis bacterial ***ghost*** vaccine to fight human blindness.
AU Eko, Francis O.; Talin, Barisani Asenbauer; ***Lubitz, Werner***

[Reprint Author]
CS Univ Vienna, Dept Med Chem, Althanstr 14,UZA2 2B522, A-1090 Vienna, Austria
werner.lubitz@univie.ac.at
SO Human Vaccines, (MAY-JUN 2008) Vol. 4, No. 3, pp. 176-183.
ISSN: 1554-8619.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 24 Sep 2008
Last Updated on STN: 24 Sep 2008
AB Trachoma is the world's leading cause of preventable disease and the third most common cause of blindness after cataract and glaucoma, affecting an estimated 84 million people and leaving 590 million at risk. As a crippling disease, trachoma causes an enormous loss of productivity and constitutes a major socioeconomic burden. Although antibiotics are effective in treating active cases of the illness, they do not prevent re-infection, which occurs with high frequency in susceptible populations. Also, once infection and pathology are established, treatment may be less effective. Another major public health challenge posed by trachoma is that a large number of infected individuals are asymptomatic and readily infect those with whom they interact. Thus, an inexpensive and easy to deliver vaccine for trachoma would be highly effective in reducing the devastation caused by this disease. Development of an effective vaccine for controlling and preventing trachoma will require an understanding of the complex immunological mechanisms that occur during infection, identifying those antigens that elicit a protective immune response and designing effective vaccine delivery systems. Significant progress has been made in the delineation of the immune correlates of protection that will form the basis of vaccine evaluation. Recent advances in chlamydial genomics and proteomics has identified a number of protective antigens or epitopes that when appropriately delivered will produce an efficacious vaccine. The challenge at this time is the development of effective methods for vaccine delivery. We have developed an effective bacterial ***ghost*** (BG) delivery system possessing intrinsic adjuvant properties and capable of simultaneously delivering multiple antigens to the immune system. Such a flexible delivery system can produce an effective vaccine that will prevent the development of trachomatous conjunctivitis and blindness. The safety and relatively cheap production cost of BG-based vaccines offer a technological and manufacturing advantage for a vaccine needed on a global scale.
TI Development of a Chlamydia trachomatis bacterial ***ghost*** vaccine to fight human blindness.
AU Eko, Francis O.; Talin, Barisani Asenbauer; ***Lubitz, Werner***
[Reprint Author]
AB. . . The challenge at this time is the development of effective methods for vaccine delivery. We have developed an effective bacterial ***ghost*** (BG) delivery system possessing intrinsic adjuvant properties and capable of simultaneously delivering multiple antigens to the immune system. Such. . .
IT . . .
IT Diseases
trachoma: bacterial disease, eye disease, epidemiology, prevention and control
Trachoma (MeSH)
IT Chemicals & Biochemicals
antigens; immune response; bacterial ***ghost*** vaccine:

immunologic-drug, vaccine
IT Miscellaneous Descriptors
proteomics; genomics; socioeconomic burden; bacterial ***ghost*** delivery system

L2 ANSWER 6 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 4
AN 2008:331389 BIOSIS <<LOGINID::20090617>>
DN PREV200800331388
TI Effective gene transfer to melanoma cells using bacterial ***ghosts*** .
AU Kudela, Pavol [Reprint Author]; Paukner, Susanne; Mayr, Ulrike Beate; Cholujova, Dana; Kohl, Gudrun; Schwarczova, Zuzana; Bizik, Jozef; Sedlak, Jan; ***Lubitz, Werner***
CS Slovak Acad Sci, Inst Canc Res, Vlarska 7, SK-83391 Bratislava, Slovakia pavol.kudela@savba.sk
SO Cancer Letters, (APR 8 2008) Vol. 262, No. 1, pp. 54-63.
CODEN: CALEDQ. ISSN: 0304-3835.
DT Article
LA English
ED Entered STN: 5 Jun 2008
Last Updated on STN: 5 Jun 2008
AB Bacterial ***ghosts*** (BG) are cell envelopes preparations of Gram-negative bacteria devoid of cytoplasmic content produced by controlled expression of PhiX174 plasmid-encoded lysis gene E. Eight melanoma cell lines were investigated for their capacity to bind and phagocyte BG derived from Escherichia coli NM522 and Mannheimia haemolytica A23. High capability to bind BG was observed in almost all of the analyzed cell lines, furthermore cells were able to take up BG independently of the used bacterial species. Further, transfection efficiency of BG loaded with DNA in vitro was measured. The Bowes cells exhibited a high expression level of GFP and the incubation of cells with plasmid loaded BG led up to 82% transfection efficiency. (C) 2007 Elsevier Ireland Ltd. All rights reserved.
TI Effective gene transfer to melanoma cells using bacterial ***ghosts*** .
AU Kudela, Pavol [Reprint Author]; Paukner, Susanne; Mayr, Ulrike Beate; Cholujova, Dana; Kohl, Gudrun; Schwarczova, Zuzana; Bizik, Jozef; Sedlak, Jan; ***Lubitz, Werner***
AB Bacterial ***ghosts*** (BG) are cell envelopes preparations of Gram-negative bacteria devoid of cytoplasmic content produced by controlled expression of PhiX174 plasmid-encoded lysis. . .
IT Miscellaneous Descriptors
bacterial ***ghost***

L2 ANSWER 7 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2009:276389 CAPLUS <<LOGINID::20090617>>
TI Bacterial ***ghosts*** as vaccine and drug delivery platforms
AU Mayr, Ulrike Beate; Koller, Verena Juliana; Lubitz, Petra; ***Lubitz,*** ***Werner***
CS Department of Medicinal Chemistry, University of Vienna, Vienna, Austria
SO Patho-Biotechnology (2008), 50-59. Editor(s): Sleator, Roy; Hill, Colin. Publisher: Landes Bioscience, Austin, Tex.
CODEN: 69LLYD; ISBN: 978-1-58706-304-6
DT Conference; General Review
LA English
AB The Bacterial ***Ghost*** (BG) Vaccine Platform Technol. represents a

particulate carrier system for protein subunit or DNA-encoded antigens endowed with intrinsic adjuvant properties. By all its biol. background BG vaccines alert the immune system with signals for a bacterial infection and induce innate and adaptive immune responses against the antigens. Presentation of subunit vaccines within the BG complex is of advantage for the recognition of the target antigens by the immune system. Delivered as particle, to facilitate the uptake by professional antigen presenting cells (APC), BG satisfy the requirement of naturally furnished adjuvant particles for submit vaccine candidates. Such BG particles have a surface make-up which is not denatured and their surface adhesins are fully functional for the interaction with cellular receptors of APCs to induce the release of natural danger signals and cytokines characteristic for infections with real pathogens. The specificity for targeting tissues or cells, the easy method of prodn. and the versatility in entrapping and packaging various compds. in different compartments of BG can be used for the creation of Advanced Drug Delivery Systems (ADDS). The original targeting functions of BG enable them to bind to and/or are being taken up by specific cells or tissues of animal, human or plant origin. The BG system represents a platform technol. for creating new qualities in nonliving carriers which can be used for the specific targeting of drugs, DNA or other active compds. such as tumor cytostatics to overcome toxic or non desired obstacles. The new system is an alternative to liposomes and may have an advantage to its higher specificity for targeting different tissues, its easy way of prodn. and its versatility in entrapping and packaging various compds. in different compartments of the carriers.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Bacterial ***ghosts*** as vaccine and drug delivery platforms

AU Mayr, Ulrike Beate; Koller, Verena Juliana; Lubitz, Petra; ***Lubitz,*** ***Werner***

AB The Bacterial ***Ghost*** (BG) Vaccine Platform Technol. represents a particulate carrier system for protein subunit or DNA-encoded antigens endowed with intrinsic adjuvant properties.. . .

ST review bacterial ***ghost*** vaccine immunomodulator

IT INDEXING IN PROGRESS

IT INDEXING IN PROGRESS

IT Pharmaceutical liposomes
(bacterial ***ghost*** system may be alternative to liposome and may have advantage to its higher specificity for targeting different tissue in animal, plant and human)

IT Antiproliferative agents
Pharmaceutical carriers
(bacterial ***ghost*** vaccine can be used for specific targeting of drug, DNA or other active compd. such as tumor cytostatic to overcome toxic or non desired obstacle in animal, plant and human)

IT Antigen-presenting cell
(bacterial ***ghost*** vaccine carrying protein subunit or DNA-encoded antigen facilitated their uptake by antigen presenting cell and induced innate and adaptive immune response in animal, plant and human)

IT Adhesins
Cytokines
Denaturation
(bacterial ***ghost*** vaccine carrying protein subunit or DNA-encoded antigen have surface which is not denatured and adhesin for interaction with antigen presenting cell releasing natural danger signal and cytokine in animal, plant and human)

IT Antigens
DNA
Human
Immunomodulators
Proteins
Vaccines
(bacterial ***ghost*** vaccine carrying protein subunit or DNA-encoded antigen may be effective in alerting immune system with signal for bacterial infection and induce innate and adaptive immune response in animal, plant and human)
IT Packaging process
(bacterial ***ghost*** vaccine showed versatility in entrapping and packaging various compds. in different compartments and can be used for creation of advanced drug delivery system in animal, plant and human)

L2 ANSWER 8 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5
AN 2007:386030 CAPLUS <<LOGINID::20090617>>
DN 147:124667
TI Bacterial ***ghosts*** as adjuvant particles
AU Riedmann, Eva M.; Kyd, Jennelle M.; Cripps, Allan W.; ***Lubitz,*** ***Werner***
CS Department of Chromosome Biology, Max F Perutz Laboratories, University of Vienna, Vienna, A-1030, Austria
SO Expert Review of Vaccines (2007), 6(2), 241-253
CODEN: ERVXAX; ISSN: 1476-0584
PB Future Drugs Ltd.
DT Journal; General Review
LA English
AB A review. The development of more advanced and effective vaccines is of great interest in modern medicine. These new-generation vaccines, based on recombinant proteins or DNA, are often less reactogenic and immunogenic than traditional vaccines. Thus, there is an urgent need for the development of new and improved adjuvants. Besides many other immunostimulatory components, the bacterial ***ghost*** (BG) system is currently under investigation as a potent vaccine delivery system with intrinsic adjuvant properties. BGs are nonliving cell envelope prepns. from Gram-neg. cells, devoid of cytoplasmic contents, while their cellular morphol. and native surface antigenic structures remain preserved. Owing to the particulate nature of BGs and the fact that they contain many well known immune-stimulating compds., BGs have the potential to enhance immune responses against ***ghost*** -delivered target antigens.
RE.CNT 133 THERE ARE 133 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Bacterial ***ghosts*** as adjuvant particles
AU Riedmann, Eva M.; Kyd, Jennelle M.; Cripps, Allan W.; ***Lubitz,*** ***Werner***
AB . . . there is an urgent need for the development of new and improved adjuvants. Besides many other immunostimulatory components, the bacterial ***ghost*** (BG) system is currently under investigation as a potent vaccine delivery system with intrinsic adjuvant properties. BGs are nonliving cell. . . and the fact that they contain many well known immune-stimulating compds., BGs have the potential to enhance immune responses against ***ghost*** -delivered target antigens.
ST review adjuvant bacterial ***ghost***
IT Immunostimulants
(adjuvants; bacterial ***ghost*** have potential to enhance immune responses against ***ghost*** -delivered target antigens because of

their particulate nature and fact that they contain many well known immune-stimulating compds.)

IT Drug delivery systems
Vaccines
(bacterial ***ghost*** system is currently under investigation as potent vaccine delivery system with intrinsic adjuvant properties)

IT Eubacteria
(***ghost*** ; bacterial ***ghost*** system is currently under investigation as potent vaccine delivery system with intrinsic adjuvant properties)

L2 ANSWER 9 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 6
AN 2007:550834 BIOSIS <<LOGINID::20090617>>
DN PREV200700554388
TI Immunogenicity and protection against genital Chlamydia infection and its complications by a multisubunit candidate vaccine.
AU Ifere, Godwin O.; He, Qing; Igietseme, Joseph U.; Ananaba, Godwin A.; Lyn, Deborah; ***Lubitz, Werner*** ; Kellar, Kathryn L.; Black, Carolyn M.; Eko, Francis O. [Reprint Author]
CS Morehouse Sch Med, Dept Microbiol Biochem and Immunol, 720 Westview Dr SW, Atlanta, GA 30310 USA
feko@msm.edu
SO Journal of Microbiology Immunology and Infection, (JUN 2007) Vol. 40, No. 3, pp. 188-200.
ISSN: 1684-1182.
DT Article
LA English
ED Entered STN: 24 Oct 2007
Last Updated on STN: 24 Oct 2007
AB Background and Purpose: Genital infections due to Chlamydia trachomatis pose a considerable public health challenge worldwide and a vaccine is urgently needed to protect against these infections. We examined whether a vaccine composed of a combination of the major outer membrane protein (MOMP) and porin B protein (PorB) of C. trachomatis would have a protective advantage over a single subunit construct.Methods: Single and multisubunit vaccines expressing MOMP and PorB were constructed and evaluated in the mouse model of genital infection. Thus, groups of female C57BL/6 mice were immunized intramuscularly with recombinant Vibrio cholerae ***ghosts*** (VCG) expressing the vaccine antigens or VCG alone and humoral and cell-mediated immune responses were evaluated.Results: Significant levels of Chlamydia-specific secretory immunoglobulin A and immunoglobulin G2a were detected in vaginal washes and serum of immunized mice. The multisubunit construct induced a significantly higher level of T-helper Type 1 response than the single subunits as measured by the amount of interferon-gamma produced by immune T cells in response to re-stimulation with ultraviolet-irradiated elementary bodies in vitro. Three weeks after the last immunization, animals were challenged intravaginally with 10(7) inclusion-forming units of C. trachomatis serovar D. There was a significant difference in the intensity and duration of vaginal shedding between the vaccine-immunized mice and controls. All the animals immunized with the multisubunit vaccine had completely resolved the infection 2 weeks post-challenge. Higher numbers of embryos were observed in vaccinated animals than in controls, indicating protection against infertility.Conclusion: These results underscore the potential, albeit moderate, vaccine advantage of the multisubunit formulation.

AU Ifere, Godwin O.; He, Qing; Igietseme, Joseph U.; Ananaba, Godwin A.; Lyn, Deborah; ***Lubitz, Werner*** ; Kellar, Kathryn L.; Black, Carolyn M.; Eko, Francis O. [Reprint Author]
AB . . in the mouse model of genital infection. Thus, groups of female C57BL/6 mice were immunized intramuscularly with recombinant Vibrio cholerae ***ghosts*** (VCG) expressing the vaccine antigens or VCG alone and humoral and cell-mediated immune responses were evaluated.Results: Significant levels of Chlamydia-specific. . .

L2 ANSWER 10 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 7
AN 2006:1073629 CAPLUS <<LOGINID::20090617>>
DN 146:43495
TI Identification of protein candidates for developing bacterial ***ghost*** vaccines against Brucella
AU Delvecchio, Vito G.; Alefantis, Tim; Ugalde, Rodolfo A.; Comerci, Diego; Marchesini, Maria Ines; Khan, Akbar; ***Lubitz, Werner*** ; Mujer, Cesar V.
CS Vital Probes, Mayfield, PA, USA
SO Methods of Biochemical Analysis (2006), 49(Microbial Proteomics), 363-377 CODEN: MBANAA; ISSN: 0076-6941
PB John Wiley & Sons, Inc.
DT Journal; General Review
LA English
AB A review on Brucella, a gram-neg. coccobacillus that causes brucellosis in both livestock and humans. Recent advances in the global identification of Brucella proteins are discussed, together with the host immune invasion strategies of Brucella, proteomes of Brucella melitensis, proteomics-based approaches to vaccine development, bacterial ***ghosts*** as new vaccine strategy against brucellosis, and future directions in proteomics-based vaccine development.
RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Identification of protein candidates for developing bacterial ***ghost*** vaccines against Brucella
AU Delvecchio, Vito G.; Alefantis, Tim; Ugalde, Rodolfo A.; Comerci, Diego; Marchesini, Maria Ines; Khan, Akbar; ***Lubitz, Werner*** ; Mujer, Cesar V.
AB . . . discussed, together with the host immune invasion strategies of Brucella, proteomes of Brucella melitensis, proteomics-based approaches to vaccine development, bacterial ***ghosts*** as new vaccine strategy against brucellosis, and future directions in proteomics-based vaccine development.

L2 ANSWER 11 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8
AN 2005:604611 CAPLUS <<LOGINID::20090617>>
DN 144:49681
TI Proteomics and Bioinformatics Strategies to Design Countermeasures against Infectious Threat Agents
AU Khan, Akbar S.; Mujer, Cesar V.; Alefantis, Timothy G.; Connolly, Joseph P.; Mayr, Ulrike Beate; Walcher, Petra; ***Lubitz, Werner*** ; DelVecchio, Vito G.
CS Defense Threat Reduction Agency Alexandria Virginia Vital Probes Incorporated, Mayfield, PA, 18433, USA
SO Journal of Chemical Information and Modeling (2006), 46(1), 111-115 CODEN: JCISD8; ISSN: 1549-9596
PB American Chemical Society
DT Journal; General Review

LA English
AB A review. The potential devastation resulting from an intentional outbreak caused by biol. warfare agents such as Brucella abortus and Bacillus anthracis underscores the need for next generation vaccines. Proteomics, genomics, and systems biol. approaches coupled with the bacterial ***ghost*** (BG) vaccine delivery strategy offer an ideal approach for developing safer, cost-effective, and efficacious vaccines for human use in a relatively rapid time frame. Crit. to any subunit vaccine development strategy is the identification of a pathogen's proteins with the greatest potential of eliciting a protective immune response. These proteins are collectively referred to as the pathogen's immunome. Proteomics provides high-resoln. identification of these immunogenic proteins using std. proteomic technologies, Western blots probed with antisera from infected patients, and the pathogen's sequenced and annotated genome. Selected immunoreactive proteins can be then cloned and expressed in nonpathogenic Gram-neg. bacteria. Subsequently, a temp. shift or chem. induction process is initiated to induce expression of the .PHI.X174 E-lysis gene, whose protein product forms an E tunnel between the inner and outer membrane of the bacteria, expelling all intracellular contents. The BG vaccine system is a proven strategy developed for many different pathogens and tested in a complete array of animal models. The BG vaccine system also has great potential for producing multi-agent vaccines for protection to multiple species in a single formulation.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AU Khan, Akbar S.; Mujer, Cesar V.; Alefantis, Timothy G.; Connolly, Joseph P.; Mayr, Ulrike Beate; Walcher, Petra; ***Lubitz, Werner*** ; DelVecchio, Vito G.
AB . . . and Bacillus anthracis underscores the need for next generation vaccines. Proteomics, genomics, and systems biol. approaches coupled with the bacterial ***ghost*** (BG) vaccine delivery strategy offer an ideal approach for developing safer, cost-effective, and efficacious vaccines for human use in a. . .

L2 ANSWER 12 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 9
AN 2005:1345121 CAPLUS <<LOGINID::20090617>>
DN 144:474476
TI Bacterial ***ghosts*** as a novel advanced targeting system for drug and DNA delivery
AU Paukner, Susanne; Stiedl, Thomas; Kudela, Pavol; Bizik, Jozef; Al Laham, Firas; ***Lubitz, Werner***
CS Department of Medical/Pharmaceutical Chemistry, University of Vienna, Vienna, A-1090, Austria
SO Expert Opinion on Drug Delivery (2006), 3(1), 11-22
CODEN: EODDAW; ISSN: 1742-5247
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. Although there are powerful drugs against infectious diseases and cancer on the market, delivery systems are needed to decrease serious toxic and noncurative side effects. In order to enhance compliance, several delivery systems such as polymeric micro- and nanoparticles, liposomal systems and erythrocyte ***ghosts*** have been developed. Bacterial ***ghosts*** representing novel advanced delivery and targeting vehicles suitable for the delivery of hydrophobic or water-sol. drugs, are the main focus of this review. They are useful nonliving carriers, as they can carry different active substances in more than one

cellular location sep. and simultaneously. Bacterial ***ghosts*** combine excellent natural or engineered adhesion properties with versatile carrier functions for drugs, proteins and DNA plasmids or DNA minicircles. The simplicity of both bacterial ***ghost*** prodn. and packaging of drugs and/or DNA makes them particularly suitable for the use as a delivery system. Further advantages of bacterial ***ghost*** delivery vehicles include high bioavailability and a long shelf life without the need of cold-chain storage due to the possibility to freeze-dry the material.

RE.CNT 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Bacterial ***ghosts*** as a novel advanced targeting system for drug and DNA delivery

AU Paukner, Susanne; Stiedl, Thomas; Kudela, Pavol; Bizik, Jozef; Al Laham, Firas; ***Lubitz, Werner***

AB . . . side effects. In order to enhance compliance, several delivery systems such as polymeric micro- and nanoparticles, liposomal systems and erythrocyte ***ghosts*** have been developed. Bacterial ***ghosts*** representing novel advanced delivery and targeting vehicles suitable for the delivery of hydrophobic or water-sol. drugs, are the main focus. . . useful nonliving carriers, as they can carry different active substances in more than one cellular location sep. and simultaneously. Bacterial ***ghosts*** combine excellent natural or engineered adhesion properties with versatile carrier functions for drugs, proteins and DNA plasmids or DNA minicircles. The simplicity of both bacterial ***ghost*** prodn. and packaging of drugs and/or DNA makes them particularly suitable for the use as a delivery system. Further advantages of bacterial ***ghost*** delivery vehicles include high bioavailability and a long shelf life without the need of cold-chain storage due to the possibility. . .

ST review bacterial ***ghost*** drug DNA delivery

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bacterial ***ghost*** showed novel advanced delivery and targeting vehicle suitable for delivery of hydrophobic or water-sol. DNA delivery, showed good bioavailability and long shelf life without need of cold-chain storage in human)

IT Drug delivery systems
(bacterial ***ghost*** showed novel advanced delivery and targeting vehicle suitable for delivery of hydrophobic or water-sol. drug delivery, showed good bioavailability and long shelf life without need of cold-chain storage in human)

IT Drug bioavailability
Human
(bacterial ***ghost*** showed novel advanced delivery and targeting vehicle suitable for delivery of hydrophobic or water-sol. drug, DNA delivery, showed good bioavailability and long shelf life without need of cold-chain storage in human)

L2 ANSWER 13 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2006:298170 BIOSIS <<LOGINID::20090617>>

DN PREV200600305144

TI Closure of bacterial ***ghost*** .

AU ***Lubitz, Werner*** [Inventor]; Paukner, Susanne [Inventor]

CS 1080 Vienna, Austria

ASSIGNEE: Werner Lubitz
PI US 06951756 20051004
SO Official Gazette of the United States Patent and Trademark Office Patents, (OCT 4 2005)
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 7 Jun 2006
Last Updated on STN: 7 Jun 2006
AB The invention relates to a method for preparing closed bacterial ***ghosts*** by means of vesicle membrane fusion and to the bacterial ***ghosts*** which can be obtained in this way. Active compounds, e.g. genetic material, cell components, pharmaceutical and agricultural active compounds and also markers or dyes can be packaged in the closed bacterial ***ghosts*** . Metabolic functions and, where appropriate, the ability of the cells to proliferate can be restored on packaging genetic material in the bacterial ***ghosts*** . The closed ***ghosts*** can be used in medicine, in the agricultural sphere and in biotechnology.
TI Closure of bacterial ***ghost*** .
AU ***Lubitz, Werner*** [Inventor]; Paukner, Susanne [Inventor]
AB The invention relates to a method for preparing closed bacterial ***ghosts*** by means of vesicle membrane fusion and to the bacterial ***ghosts*** which can be obtained in this way. Active compounds, e.g. genetic material, cell components, pharmaceutical and agricultural active compounds and also markers or dyes can be packaged in the closed bacterial ***ghosts*** . Metabolic functions and, where appropriate, the ability of the cells to proliferate can be restored on packaging genetic material in the bacterial ***ghosts*** . The closed ***ghosts*** can be used in medicine, in the agricultural sphere and in biotechnology.
IT Major Concepts
Pharmacology; Methods and Techniques; Agriculture; Bioprocess Engineering
IT Chemicals & Biochemicals
bacterial ***ghosts*** : pharmaceutical adjunct-drug
IT Methods & Equipment
vesicle membrane fusion-mediated bacterial ***ghost*** production method: laboratory techniques

L2 ANSWER 14 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:120755 CAPLUS <<LOGINID::20090617>>
DN 142:225686
TI Sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions
IN ***Lubitz, Werner***
PA Austria
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005011713	A1	20050210	WO 2004-EP8790	20040805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE	10335796	A1	20050303	DE 2003-10335796	20030805
AU	2004260620	A1	20050210	AU 2004-260620	20040805
AU	2004260620	B2	20080124		
CA	2534612	A1	20050210	CA 2004-2534612	20040805
EP	1656149	A1	20060517	EP 2004-763831	20040805

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

NZ	545232	A	20081224	NZ 2004-545232	20040805
US	20060286126	A1	20061221	US 2006-567426	20060516
PRAI DE	2003-10335796	A	20030805		
WO	2004-EP8790	W	20040805		

AB The invention relates to a method for producing sealed bacterial ***ghosts*** using the specific interaction between partners of a binding pair. The ***ghosts*** can be loaded with therapeutically useful substances and used as carriers. The inventive sealed ***ghosts*** can be used in medicine, agriculture, and biotechnol. ***Ghosts*** are formed by inducing expression of the E gene, which causes membrane lysis. The ***ghosts*** are then derivatized with a member of a binding pair, e.g. biotin, or a streptavidin-binding peptide. Biotinylation may be via an enzymic biotinylation site incorporated into the E gene product. The derivatized ***ghosts*** are then mixed with lipid vesicles present the other member of the binding pair, e.g. streptavidin. The interaction results in the binding of the lipid vesicles to the ***ghosts*** . Sealed ***ghosts*** can be captured using the ligand immobilized on a suitable carrier.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions

IN ***Lubitz, Werner***

AB The invention relates to a method for producing sealed bacterial ***ghosts*** using the specific interaction between partners of a binding pair. The ***ghosts*** can be loaded with therapeutically useful substances and used as carriers. The inventive sealed ***ghosts*** can be used in medicine, agriculture, and biotechnol. ***Ghosts*** are formed by inducing expression of the E gene, which causes membrane lysis. The ***ghosts*** are then derivatized with a member of a binding pair, e.g. biotin, or a streptavidin-binding peptide. Biotinylation may be via an enzymic biotinylation site incorporated into the E gene product. The derivatized ***ghosts*** are then mixed with lipid vesicles present the other member of the binding pair, e.g. streptavidin. The interaction results in the binding of the lipid vesicles to the ***ghosts*** . Sealed ***ghosts*** can be captured using the ligand immobilized on a suitable carrier.

ST bacteria membrane ***ghost*** sealing lipid vesicle affinity interaction; membrane biotin vesicle streptavidin bacteria ***ghost*** sealing

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(E; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Drug delivery systems
(bacterial ***ghosts*** as; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Transformation, genetic
(bacterial ***ghosts*** for delivery of nucleic acids in; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Agrochemicals
Drugs
Dyes
Organelle
(bacterial ***ghosts*** for delivery of; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Nucleic acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bacterial ***ghosts*** for delivery of; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Protein motifs
(biotinylation, lysis proteins contg.; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Protoplast and Spheroplast
(cell ***ghost*** ; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Virion structure
(envelope, sealing of membrane ***ghosts*** with; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Antibodies and Immunoglobulins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fragments, in affinity binding of membrane vesicles to bacterial ***ghosts*** ; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Agglutinins and Lectins
Antibodies and Immunoglobulins
Avidins
Carbohydrates, biological studies
Haptens
Receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in affinity binding of membrane vesicles to bacterial ***ghosts*** ; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Eubacteria
(membrane ***ghosts*** ; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Proteins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(membrane, incorporation into bacterial ***ghosts*** of; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Immobilization, molecular or cellular
(of bacterial ***ghosts*** ; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Gram-negative bacteria
(prepn. of membrane ***ghosts*** from; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Agriculture and Agricultural chemistry
Biotechnology
Medicine
(sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Liposomes
(sealing of membrane ***ghosts*** with; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Lipids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(vesicles, sealing of membrane ***ghosts*** with; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT 58-85-5D, Biotin, analogs, conjugates with proteins 9013-20-1, Streptavidin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in affinity binding of membrane vesicles to bacterial ***ghosts*** ; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT 842177-75-7 842177-76-8 842177-77-9 842177-78-0 842177-79-1 842177-80-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT 842138-49-2
RL: PRP (Properties)
(unclaimed sequence; sealing of bacterial ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

L2 ANSWER 15 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 10

AN 2005:436612 BIOSIS <<LOGINID::20090617>>

DN PREV200510222102

TI Bacterial ***ghosts*** as an oral vaccine: a single dose of Escherichia coli O157 : H7 bacterial ***ghosts*** protects mice against lethal challenge.

AU Mayr, Ulrike Beate [Reprint Author]; Haller, Christoph; Haidinger, Wolfgang; Atrasheuskaya, Alena; Bukin, Eugenij; ***Lubitz, Werner*** ; Ignatyev, Georgy

CS Univ Vienna, Fac Life Sci, Dept Med Pharmaceut Sci, Althanstr 14,UZAII,2B522, A-1090 Vienna, Austria
ulrike.beate.mayr@univie.ac.at

SO Infection and Immunity, (AUG 2005) Vol. 73, No. 8, pp. 4810-4817.
CODEN: INFIBR. ISSN: 0019-9567.
DT Article
LA English
ED Entered STN: 26 Oct 2005
Last Updated on STN: 26 Oct 2005
AB Enterohemorrhagic Escherichia coli (EHEC) is a bacterial pathogen that is associated with several life-threatening diseases for humans. The combination of protein E-mediated cell lysis to produce EHEC ***ghosts*** and staphylococcal nuclease A to degrade DNA was used for the development of an oral EHEC vaccine. The lack of genetic material in the oral EHEC bacterial- ***ghost*** vaccine abolished any hazard of horizontal gene transfer of resistance genes or pathogenic islands to resident gut flora. Intragastric immunization of mice with EHEC ***ghosts*** without the addition of any adjuvant induced cellular and humoral immunity. Immunized mice challenged at day 55 showed 86% protection against lethal challenge with a heterologous EHEC strain after single-dose oral immunization and 93.3% protection after one booster at day 28, whereas the controls showed 26.7% and 30% survival, respectively. These results indicate that it is possible to develop an efficacious single-dose oral EHEC bacterial- ***ghost*** vaccine.
TI Bacterial ***ghosts*** as an oral vaccine: a single dose of Escherichia coli O157 : H7 bacterial ***ghosts*** protects mice against lethal challenge.
AU Mayr, Ulrike Beate [Reprint Author]; Haller, Christoph; Haidinger, Wolfgang; Atrasheuskaya, Alena; Bukin, Eugenij; ***Lubitz, Werner*** ; Ignatyev, Georgy
AB. . . pathogen that is associated with several life-threatening diseases for humans. The combination of protein E-mediated cell lysis to produce EHEC ***ghosts*** and staphylococcal nuclease A to degrade DNA was used for the development of an oral EHEC vaccine. The lack of genetic material in the oral EHEC bacterial- ***ghost*** vaccine abolished any hazard of horizontal gene transfer of resistance genes or pathogenic islands to resident gut flora. Intragastric immunization of mice with EHEC ***ghosts*** without the addition of any adjuvant induced cellular and humoral immunity. Immunized mice challenged at day 55 showed 86% protection. . . showed 26.7% and 30% survival, respectively. These results indicate that it is possible to develop an efficacious single-dose oral EHEC bacterial- ***ghost*** vaccine.

L2 ANSWER 16 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 11
AN 2005:326140 BIOSIS <<LOGINID::20090617>>
DN PREV200510118104
TI Comparative immunogenicity of the Hepatitis B virus core 149 antigen displayed on the inner and outer membrane of bacterial ***ghosts*** .
AU Jechlinger, Wolfgang [Reprint Author]; Haller, Christoph; Resch, Stephanie; Hofmann, Andrea; Szostak, Michael P.; ***Lubitz, Werner***
CS Univ Vet Med, Inst Bacteriol Mycol and Hyg, Dept Pathobiol, Vet Pl 1, A-1210 Vienna, Austria
Wolfgang.Jechlinger@vu-wien.ac.at
SO Vaccine, (MAY 20 2005) Vol. 23, No. 27, pp. 3609-3617.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 25 Aug 2005
Last Updated on STN: 25 Aug 2005

AB Two membrane compartments of Escherichia coli ***ghosts*** , representing empty bacterial cell envelopes, were investigated as carriers of foreign antigens. By subcutaneous immunisation of mice the immunogenicity of bacterial ***ghosts*** carrying the Hepatitis B virus core 149 protein (HBcAg-149) as model antigen anchored either in the inner or the outer membrane of E. coli was compared. Both systems induced significant immune responses against the foreign target antigen, the HBcAg-149, in mice. Results indicate that bacterial ***ghosts*** provide an excellent carrier system for antigen delivery. (c) 2005 Elsevier Ltd. All rights reserved.

TI Comparative immunogenicity of the Hepatitis B virus core 149 antigen displayed on the inner and outer membrane of bacterial ***ghosts*** .

AU Jechlinger, Wolfgang [Reprint Author]; Haller, Christoph; Resch, Stephanie; Hofmann, Andrea; Szostak, Michael P.; ***Lubitz, Werner***

AB Two membrane compartments of Escherichia coli ***ghosts*** , representing empty bacterial cell envelopes, were investigated as carriers of foreign antigens. By subcutaneous immunisation of mice the immunogenicity of bacterial ***ghosts*** carrying the Hepatitis B virus core 149 protein (HBcAg-149) as model antigen anchored either in the inner or the outer. . . compared. Both systems induced significant immune responses against the foreign target antigen, the HBcAg-149, in mice. Results indicate that bacterial ***ghosts*** provide an excellent carrier system for antigen delivery. (c) 2005 Elsevier Ltd. All rights reserved.

IT Methods & Equipment
subcutaneous immunization: therapeutic and prophylactic techniques, clinical techniques

IT Miscellaneous Descriptors
immune responses; antigen delivery; immunogenicity; bacterial ***ghosts***

L2 ANSWER 17 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 12

AN 2005:329005 BIOSIS <<LOGINID::20090617>>

DN PREV200510106667

TI Bacterial ***ghosts*** as antigen delivery vehicles.

AU Mayr, Ulrike Beate; Walcher, Petra; Azimpour, Chakameh; Riedmann, Eva; Haller, Christoph; ***Lubitz, Werner*** [Reprint Author]

CS Univ Vienna, Dept Med Pharmaceut Chem, Waehringer Guertel 18, A-1090 Vienna, Austria
Wemer.Lubitz@univie.ac.at

SO Advanced Drug Delivery Reviews, (JUN 17 2005) Vol. 57, No. 9, pp. 1381-1391.
CODEN: ADDREP. ISSN: 0169-409X.

DT Article

LA English

ED Entered STN: 25 Aug 2005
Last Updated on STN: 31 Dec 2008

AB The bacterial ***ghost*** system is a novel vaccine delivery system unusual in that it combines excellent natural intrinsic adjuvant properties with versatile carrier functions for foreign antigens. The efficient tropism of bacterial ***ghosts*** (BG) for antigen presenting cells promotes the generation of both cellular and Immoral responses to heterologous antigens and carrier envelope structures. The simplicity of both BG production and packaging of (multiple) target antigens makes them particularly suitable for use as combination vaccines. Further advantages of BG vaccines include a long shelf-life without the

need of cold-chain storage due to their freeze-dried status, they are safe as they do not involve host DNA or live organisms, they exhibit improved potency with regard to target antigens compared to conventional approaches, they are versatile with regards to DNA or protein antigen choice and size, and as a delivery system they offer high bioavailability. (c) 2005 Elsevier B.V. All rights reserved.

TI Bacterial ***ghosts*** as antigen delivery vehicles.

AU Mayr, Ulrike Beate; Walcher, Petra; Azimpour, Chakameh; Riedmann, Eva; Haller, Christoph; ***Lubitz, Werner*** [Reprint Author]

AB The bacterial ***ghost*** system is a novel vaccine delivery system unusual in that it combines excellent natural intrinsic adjuvant properties with versatile carrier functions for foreign antigens. The efficient tropism of bacterial ***ghosts*** (BG) for antigen presenting cells promotes the generation of both cellular and Immoral responses to heterologous antigens and carrier envelope. . .

IT . . .
Pharmacology; Immune System (Chemical Coordination and Homeostasis)

IT Chemicals & Biochemicals
heterologous antigens; foreign antigen; DNA vaccine: immunologic-drug, vaccine; bacterial ***ghost*** ; bacterial envelope

L2 ANSWER 18 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 13

AN 2005:166878 BIOSIS <<LOGINID::20090617>>

DN PREV200500166891

TI Immobilization of plasmid DNA in bacterial ***ghosts*** .

AU Mayrhofer, Peter; Tabrizi, Chakameh Azimpour; Walcher, Petra; Haidinger, Wolfgang; Jechlinger, Wolfgang [Reprint Author]; ***Lubitz, Werner***

CS Dept PathobiolInst Bacteriol Mycol and Hyg, Univ Vet Med, Vet Pl 1, A-1210, Vienna, Austria
Wolfgang.Jechlinger@vu-wien.ac.at

SO Journal of Controlled Release, (February 16 2005) Vol. 102, No. 3, pp. 725-735. print.
ISSN: 0168-3659 (ISSN print).

DT Article

LA English

ED Entered STN: 27 Apr 2005
Last Updated on STN: 27 Apr 2005

AB The development of novel delivery vehicles is crucial for the improvernent of DNA vaccine efficiency. In this report, we describe a new platform technology, which is based on the immobilization of plasmid DNA in the cytoplasmic membrane of a bacterial carrier. This technology retains plasmid DNA (Self-Immobilizing Plasmid, pSIP) in the host envelope complex due to a specific protein/DNA interaction during and after protein E-mediated lysis. The resulting bacterial ***ghosts*** (empty bacterial envelopes) loaded with pDNA were analyzed in detail by real time PCR assays. We could verify that pSIP plasmids were retained in the pellets of lysed Escherichia coli cultures indicating that they are efficiently anchored in the inner membrane of bacterial ***ghosts*** . In contrast, a high percentage of control plasmids that lack essential features of the self-immobilization system were expelled in the culture broth during the lysis process. We believe that the combination of this plasmid immobilization procedure and the protein E-mediated lysis technology represents an efficient in vivo technique for the production of non-living DNA carrier vehicles. In conclusion, we present a "self-loading", non-living bacterial DNA delivery vector for vaccination endowed with intrinsic adjuvant properties of the Gram-negative bacterial

cell envelope. Copyright 2004 Elsevier B.V. All rights reserved.
TI Immobilization of plasmid DNA in bacterial ***ghosts*** .
AU Mayrhofer, Peter; Tabrizi, Chakameh Azimpour; Walcher, Petra; Haidinger, Wolfgang; Jechlinger, Wolfgang [Reprint Author]; ***Lubitz, Werner***
AB . . in the host envelope complex due to a specific protein/DNA interaction during and after protein E-mediated lysis. The resulting bacterial ***ghosts*** (empty bacterial envelopes) loaded with pDNA were analyzed in detail by real time PCR assays. We could verify that pSIP. . . in the pellets of lysed Escherichia coli cultures indicating that they are efficiently anchored in the inner membrane of bacterial ***ghosts*** . In contrast, a high percentage of control plasmids that lack essential features of the self-immobilization system were expelled in the. . .
IT Methods & Equipment
DNA delivery vector: drug delivery device; bacterial ***ghost*** : drug delivery device; real-time polymerase chain reaction [real-time PCR]: genetic techniques, laboratory techniques

L2 ANSWER 19 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1024716 CAPLUS <<LOGINID::20090617>>
DN 144:93945
TI Minicircle DNA Immobilized in Bacterial ***Ghosts*** : In vivo Production of Safe Non-Viral DNA Delivery Vehicles
AU Jechlinger, Wolfgang; Azimpour Tabrizi, Chakameh; ***Lubitz, Werner*** ; Mayrhofer, Peter
CS Institute of Microbiology and Genetics, Section Microbiology and Biotechnology, University of Vienna, Vienna, Austria
SO Journal of Molecular Microbiology and Biotechnology (2005), 8(4), 222-231 CODEN: JMMBFF; ISSN: 1464-1801
PB S. Karger AG
DT Journal
LA English
AB DNA as an active agent is among the most promising technologies for vaccination and therapy. However, plasmid backbone sequences needed for the prodn. of pDNA in bacteria are dispensable, reduce the efficiency of the DNA agent and, most importantly, represent a biol. safety risk. In this report we describe a novel technique where a site-specific recombination system based on the ParA resolvase was applied to a self-immobilizing plasmid system (SIP). In addn., this system was combined with the protein E-specific lysis technol. to produce non-living bacterial carrier vehicles loaded with minicircle DNA. The in vivo recombination process completely divided an origin plasmid into a minicircle and a miniplasmid. The replicative miniplasmid contg. the origin of replication and the antibiotic resistance gene was lost during the subsequently induced PhiX174 gene E-mediated lysis process, which results in bacterial ***ghosts*** . The minicircle DNA was retained in these empty bacterial cell envelopes during the lysis process via the specific interaction of a membrane anchored protein with the minicircle DNA. Using this novel platform technol., a DNA delivery vehicle - consisting of a safe bacterial carrier with known adjuvant properties and minicircle DNA with an optimized safety profile - can be produced in vivo in a continuous process. Furthermore, this study provides the basis for the development of an efficient in vitro minicircle purifn. process.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Minicircle DNA Immobilized in Bacterial ***Ghosts*** : In vivo Production of Safe Non-Viral DNA Delivery Vehicles

AU Jechlinger, Wolfgang; Azimpour Tabrizi, Chakameh; ***Lubitz, Werner***
; Mayrhofer, Peter
AB . . . and the antibiotic resistance gene was lost during the subsequently induced PhiX174 gene E-mediated lysis process, which results in bacterial ***ghosts*** . The minicircle DNA was retained in these empty bacterial cell envelopes during the lysis process via the specific interaction of. . .
ST minicircle DNA immobilized bacteria ***ghost*** viral delivery
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-resolving; minicircle DNA immobilized in bacterial ***ghosts***
as safe non-viral DNA delivery vehicles)
IT Escherichia coli
Eubacteria
Genetic vectors
Immobilization, molecular or cellular
Transformation, genetic
Vaccines
(minicircle DNA immobilized in bacterial ***ghosts*** as safe
non-viral DNA delivery vehicles)

L2 ANSWER 20 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 14
AN 2005:66560 CAPLUS <<LOGINID::20090617>>
DN 143:1800
TI DNA-loaded bacterial ***ghosts*** efficiently mediate reporter gene transfer and expression in macrophages
AU Paukner, Susanne; Kudela, Pavol; Kohl, Gudrun; Schlapp, Tobias; Friedrichs, Sonja; ***Lubitz, Werner***
CS Institute of Microbiology and Genetics, Vienna University Biocenter, Vienna, A-1030, Austria
SO Molecular Therapy (2005), 11(2), 215-223
CODEN: MTOHCK; ISSN: 1525-0016
PB Elsevier
DT Journal
LA English
AB There is a demand for efficient and safe DNA delivery vehicles mediating gene transfer and expression. We present bacterial ***ghosts*** as a novel platform technol. for DNA delivery and targeting of macrophages. Bacterial ***ghosts*** are cell envelopes of gram-neg. bacteria that are devoid of the cytoplasmic content. Escherichia coli ***ghosts*** were loaded with plasmid DNA and linear double-stranded DNA. Confocal laser scanning microscopy and flow cytometry confirmed that the DNA localized to the inner lumen of bacterial ***ghosts*** and was not assocd. with the outer surface of the bacteria. Up to .apprx.6000 plasmids could be loaded per single ***ghost*** and the amt. of loaded DNA correlated with the DNA concn. used for loading. E. coli ***ghosts*** loaded with plasmids encoding the enhanced green fluorescent protein (EGFP) targeted efficiently murine macrophages (RAW264.7) and mediated effective gene transfer. The EGFP was expressed by more than 60% of the macrophages as measured by flow cytometry detecting the green fluorescence and immunocytochem. staining with antibodies specific for EGFP.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI DNA-loaded bacterial ***ghosts*** efficiently mediate reporter gene transfer and expression in macrophages
AU Paukner, Susanne; Kudela, Pavol; Kohl, Gudrun; Schlapp, Tobias;

Friedrichs, Sonja; ***Lubitz, Werner***

AB There is a demand for efficient and safe DNA delivery vehicles mediating gene transfer and expression. We present bacterial ***ghosts*** as a novel platform technol. for DNA delivery and targeting of macrophages. Bacterial ***ghosts*** are cell envelopes of gram-neg. bacteria that are devoid of the cytoplasmic content. Escherichia coli ***ghosts*** were loaded with plasmid DNA and linear double-stranded DNA. Confocal laser scanning microscopy and flow cytometry confirmed that the DNA localized to the inner lumen of bacterial ***ghosts*** and was not assocd. with the outer surface of the bacteria. Up to .apprx.6000 plasmids could be loaded per single ***ghost*** and the amt. of loaded DNA correlated with the DNA concn. used for loading. E. coli ***ghosts*** loaded with plasmids encoding the enhanced green fluorescent protein (EGFP) targeted efficiently murine macrophages (RAW264.7) and mediated effective gene transfer.. . .

ST gene transfer DNA plasmid bacteria Escherichia ***ghost*** macrophage mouse

IT Cell envelope
(bacterial ***ghosts*** ; plasmid and linear dsDNA-loaded bacterial ***ghosts*** efficiently mediate reporter gene transfer and expression in mouse macrophages)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(double-stranded, linear; plasmid and linear dsDNA-loaded bacterial ***ghosts*** efficiently mediate reporter gene transfer and expression in mouse macrophages)

IT Escherichia coli
Macrophage
Plasmid vectors
Transformation, genetic
(plasmid and linear dsDNA-loaded bacterial ***ghosts*** efficiently mediate reporter gene transfer and expression in mouse macrophages)

L2 ANSWER 21 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 15

AN 2005:208180 BIOSIS <<LOGINID::20090617>>

DN PREV200500207939

TI Bacterial ***ghosts*** as novel efficient targeting vehicles for DNA delivery to the human monocyte-derived dendritic cells.

AU Kudela, Pavol [Reprint Author]; Paukner, Susanne; Mayr, Ulrike Beate; Cholujova, Dana; Schwarczova, Zuzana; Sedlak, Jan; Bizik, Jozef; ***Lubitz, Werner***

CS Canc Res Inst, Slovak Acad Sci, Vlarska 7, SK-83391, Bratislava, Slovakia pavol.kudela@savba.sk

SO Journal of Immunotherapy, (March 2005) Vol. 28, No. 2, pp. 136-143. print. ISSN: 1524-9557 (ISSN print).

DT Article

LA English

ED Entered STN: 1 Jun 2005
Last Updated on STN: 1 Jun 2005

AB Recombinant bacterial ***ghosts*** loaded with plasmids were tested as an antigen delivery system and as a potential mediator of maturation for human monocyte-derived dendritic cells (DCs). Bacterial ***ghosts*** are cell envelopes derived from Gram-negative bacteria; the intracellular content is released by the controlled expression of plasmid-encoded lysis gene E of PhiX174. All the cell surface structures of the native bacteria, including the outer membrane proteins, adhesins, LPS, lipid A,

and peptidoglycans, are preserved. Co-incubation of immature DCs with ***ghosts*** resulted in decreased expression of CDla, CD80, and CD83 molecules, while addition of maturation mix (TNF-alpha, IL-Ibeta, IL-6, and PGE2) to the cultures enhanced expression of these molecules. No marked changes were observed in the expression of the CD11c, CD40, and CD86 surface molecules. The exposure of DCs to ***ghosts*** in combination with maturation mix resulted in a nonsignificant increase in their ability to activate T cells. DCs co-incubated with bacterial ***ghosts*** carrying plasmids encoding GFP in combination with maturation mix exhibited high expression levels of GFP (up to 85%). These results indicate that in addition to their well-established use as vaccines, bacterial ***ghosts*** can also be used as carriers of nucleic acid-encoded antigens.

TI Bacterial ***ghosts*** as novel efficient targeting vehicles for DNA delivery to the human monocyte-derived dendritic cells.

AU Kudela, Pavol [Reprint Author]; Paukner, Susanne; Mayr, Ulrike Beate; Cholujova, Dana; Schwarczova, Zuzana; Sedlak, Jan; Bizik, Jozef; ***Lubitz, Werner***

AB Recombinant bacterial ***ghosts*** loaded with plasmids were tested as an antigen delivery system and as a potential mediator of maturation for human monocyte-derived dendritic cells (DCs). Bacterial ***ghosts*** are cell envelopes derived from Gram-negative bacteria; the intracellular content is released by the controlled expression of plasmid-encoded lysis gene. . . native bacteria, including the outer membrane proteins, adhesins, LPS, lipid A, and peptidoglycans, are preserved. Co-incubation of immature DCs with ***ghosts*** resulted in decreased expression of CDla, CD80, and CD83 molecules, while addition of maturation mix (TNF-alpha, IL-Ibeta, IL-6, and PGE2). . . marked changes were observed in the expression of the CD11c, CD40, and CD86 surface molecules. The exposure of DCs to ***ghosts*** in combination with maturation mix resulted in a nonsignificant increase in their ability to activate T cells. DCs co-incubated with bacterial ***ghosts*** carrying plasmids encoding GFP in combination with maturation mix exhibited high expression levels of GFP (up to 85%). These results indicate that in addition to their well-established use as vaccines, bacterial ***ghosts*** can also be used as carriers of nucleic acid-encoded antigens.

IT . . .
Immune System (Chemical Coordination and Homeostasis); Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Parts, Structures, & Systems of Organisms
bacterial ***ghost*** ; dendritic cell: immune system; monocyte: blood and lymphatics, immune system

IT Chemicals & Biochemicals
adhesins; antigen 106; lipid A; lipopolysaccharide;. . .

L2 ANSWER 22 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:27926 CAPLUS <<LOGINID::20090617>>

DN 142:424714

TI Modulation of gene expression by promoter mutants of the .lambda.cI857/pRM/pR system

AU Jechlinger, Wolfgang; Glocker, Julia; Haidinger, Wolfgang; Matis, Alexander; Szostak, Michael P.; ***Lubitz, Werner***

CS Institute of Microbiology and Genetics, UZAII, University of Vienna, Vienna, A-1090, Austria

SO Journal of Biotechnology (2005), 116(1), 11-20
CODEN: JBITD4; ISSN: 0168-1656

PB Elsevier B.V.

DT Journal
LA English
AB Gene expression driven by the pR promoter of the .lambda.cI857/pRM/pR system results from inactivation of the temp.-sensitive CI857 repressor. The CI857 repressor, whose gene is transcribed by the divergently orientated pRM promoter, is destabilized at temps. above 30 .degree.C. In this study, the .lambda.cI857/pRM/pR system was modified by the introduction of a single (A-32G) and a double mutation (A-32G and T-41C). The mutated .lambda.pR expression modules, 32G and 32G/41C, tightly repressed the highly lethal phage PhiX174 lysis gene E at temps. up to 37 and 39 .degree.C, resp. Expression of protein E and subsequent lysis of Escherichia coli was still induced by a temp. up-shift to 42 .degree.C. The impact of the mutations on gene expression levels driven by the .lambda.pR and pRM promoters was evaluated at various temps. using the lacZ reporter gene. Results indicate that the A-32G mutation confers a .lambda.pR promoter-down phenotype. The addnl. increase in the temp. stability of the 32G/41C expression system is due to the T-41C mutation leading to a higher pRM activity. The described .lambda.pR expression modules can be used to obtain a defined expression level at a given temp. and to tightly repress in particular highly lethal genes at different bacterial growth temps.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AU Jechlinger, Wolfgang; Glocker, Julia; Haidinger, Wolfgang; Matis, Alexander; Szostak, Michael P.; ***Lubitz, Werner***
IT Genetic engineering
(modulation of gene expression by promoter mutants of .lambda.cI857/pRM/pR system for potential use in producing bacterial ***ghosts***)
IT Cytolysis
(temp.-dependent; modulation of gene expression by promoter mutants of .lambda.cI857/pRM/pR system for potential use in producing bacterial ***ghosts***)

L2 ANSWER 23 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 16
AN 2004:309651 BIOSIS <<LOGINID::20090617>>
DN PREV200400309669
TI Bacterial ***ghosts*** are an efficient delivery system for DNA vaccines.
AU Ebensen, Thomas; Paukner, Susanne; Link, Claudia; Kudela, Pavol; de Domenico, Carola; ***Lubitz, Werner*** ; Guzman, Carlos A. [Reprint Author]
CS Gesell Biotechnol ForschungDiv MicrobiolVaccine Res Grp, German Re Ctr Biotechnol, Mascheroder Weg 1, D-38124, Braunschweig, Germany
cag@gbf.de
SO Journal of Immunology, (June 1 2004) Vol. 172, No. 11, pp. 6858-6865. print.
ISSN: 0022-1767 (ISSN print).
DT Article
LA English
ED Entered STN: 7 Jul 2004
Last Updated on STN: 7 Jul 2004
AB Mass implementation of DNA vaccines is hindered by the requirement of high plasmid dosages and poor immunogenicity. We evaluated the capacity of Mannheimia haemolytica ***ghosts*** as delivery system for DNA vaccines. In vitro studies showed that bacterial ***ghosts*** loaded

with a plasmid carrying the green fluorescent protein-encoding gene (pEGFP-N1) are efficiently taken up by APC, thereby leading to high transfection rates (52-60%). Vaccination studies demonstrated that ***ghost*** -mediated delivery by intradermal or i.m. route of a eukaryotic expression plasmid containing the gene coding for beta-galactosidase under the control of the CMV immediate early gene promoter (pCMVbeta) stimulates more efficient Ag-specitic Immoral and cellular (CD4+ and CD8+) immune responses than naked DNA in BALB/c mice. The use of ***ghosts*** also allows modulating the major Th response from a mixed Th1/Th2 to a more dominant Th2 pattern. Intravenous immunization with dendritic cells loaded ex vivo with pCMVbeta-containing ***ghosts*** also resulted in the elicitation of beta-galactosidase-specific responses. This suggests that dendritic cells play an important role in the stimulation of immune responses when bacterial ***ghosts*** are used as a DNA delivery system. Bacterial ***ghosts*** not only target the DNA vaccine construct to APC, but also provide a strong danger signal, acting as natural adjuvants, thereby promoting efficient maturation and activation of dendritic cells. Thus, bacterial ***ghosts*** constitute a promising technology platform for the development of more efficient DNA vaccines.

TI Bacterial ***ghosts*** are an efficient delivery system for DNA vaccines.

AU Ebensen, Thomas; Paukner, Susanne; Link, Claudia; Kudela, Pavol; de Domenico, Carola; ***Lubitz, Werner*** ; Guzman, Carlos A. [Reprint Author]

AB. . . vaccines is hindered by the requirement of high plasmid dosages and poor immunogenicity. We evaluated the capacity of Mannheimia haemolytica ***ghosts*** as delivery system for DNA vaccines. In vitro studies showed that bacterial ***ghosts*** loaded with a plasmid carrying the green fluorescent protein-encoding gene (pEGFP-N1) are efficiently taken up by APC, thereby leading to high transfection rates (52-60%). Vaccination studies demonstrated that ***ghost*** -mediated delivery by intradermal or i.m. route of a eukaryotic expression plasmid containing the gene coding for beta-galactosidase under the control. . . more efficient Ag-specitic Immoral and cellular (CD4+ and CD8+) immune responses than naked DNA in BALB/c mice. The use of ***ghosts*** also allows modulating the major Th response from a mixed Th1/Th2 to a more dominant Th2 pattern. Intravenous immunization with dendritic cells loaded ex vivo with pCMVbeta-containing ***ghosts*** also resulted in the elicitation of beta-galactosidase-specific responses. This suggests that dendritic cells play an important role in the stimulation of immune responses when bacterial ***ghosts*** are used as a DNA delivery system. Bacterial ***ghosts*** not only target the DNA vaccine construct to APC, but also provide a strong danger signal, acting as natural adjuvants, thereby promoting efficient maturation and activation of dendritic cells. Thus, bacterial ***ghosts*** constitute a promising technology platform for the development of more efficient DNA vaccines.

IT . . .

IT Parts, Structures, & Systems of Organisms
antigen-presenting cells: immune system

IT Chemicals & Biochemicals
DNA vaccines: immunologic-drug, immunostimulant-drug; bacterial ***ghosts***

L2 ANSWER 24 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 17

AN 2004:442034 BIOSIS <<LOGINID::20090617>>
DN PREV200400446735
TI Bacterial ***ghost*** technology for pesticide delivery.
AU Hatfaludi, Tamas [Reprint Author]; Liska, Martina; Zellinger, Daniela; Ousman, Jarju Pa; Szostak, Michael; Ambrus, Arpad; Jalava, Katri; ***Lubitz, Werner***
CS Inst Microbiol and GenetSect Microbiol and Biotechnol, Univ Vienna, UZAII 2B522 Althanstr 14, A-1090, Vienna, Austria
tamas.hatfaludi@univie.ac.at
SO Journal of Agricultural and Food Chemistry, (September 8 2004) Vol. 52, No. 18, pp. 5627-5634. print.
CODEN: JAFCAU. ISSN: 0021-8561.
DT Article
LA English
ED Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004
AB Bacterial ***ghosts*** are nondenaturated empty cell envelopes of Gram-negative bacteria produced by E-mediated lysis. Such envelopes from the plant-adhering bacterium Pectobacterium cypripedii were tested for their ability to adhere to plant material and to be used as carriers for pesticide delivery. We show, using fluorescence-labeled P. cypripedii ***ghosts*** , that depending on the target plants 55 or 10% (rice or soya, respectively) of the applied bacterial ***ghosts*** was retained on the leaves after heavy simulated rain (84 mm). Furthermore, the bacterial ***ghosts*** could be loaded with the lipophilic triazole fungicide tebuconazole. In subsequent plant experiments in the glass house, the efficacy of the loaded bacterial ***ghost*** for resistance to rainfall and the protective and curative effects against the pathogens Erysiphe graminis, Leptosphaeria nodorum, and Pyrenophora teres on barley and wheat and against Sphaerotheca fuliginea on cucumber were tested. The bacterial ***ghosts*** were compared primarily with a commercial tebuconazole formulation, a wettable powder, as it has similar physical characteristics. The comparison revealed similar effects and showed consistently higher or comparable efficacy against the pathogens. The standard operational comparison with the most protective, cereal specific emulsion of oil in water displayed that the bacterial ***ghosts*** had equal to or lower efficacy than the emulsion. This study confirmed the potential of bacterial ***ghost*** platform technology as a new alternative carrier system for pesticides.
TI Bacterial ***ghost*** technology for pesticide delivery.
AU Hatfaludi, Tamas [Reprint Author]; Liska, Martina; Zellinger, Daniela; Ousman, Jarju Pa; Szostak, Michael; Ambrus, Arpad; Jalava, Katri; ***Lubitz, Werner***
AB Bacterial ***ghosts*** are nondenaturated empty cell envelopes of Gram-negative bacteria produced by E-mediated lysis. Such envelopes from the plant-adhering bacterium Pectobacterium cypripedii. . . to adhere to plant material and to be used as carriers for pesticide delivery. We show, using fluorescence-labeled P. cypripedii ***ghosts*** , that depending on the target plants 55 or 10% (rice or soya, respectively) of the applied bacterial ***ghosts*** was retained on the leaves after heavy simulated rain (84 mm). Furthermore, the bacterial ***ghosts*** could be loaded with the lipophilic triazole fungicide tebuconazole. In subsequent plant experiments in the glass house, the efficacy of the loaded bacterial ***ghost*** for resistance to rainfall and the protective and curative effects against the pathogens Erysiphe graminis, Leptosphaeria nodorum, and Pyrenophora teres on barley and wheat and against Sphaerotheca fuliginea on cucumber were tested. The bacterial

ghosts were compared primarily with a commercial tebuconazole formulation, a wettable powder, as it has similar physical characteristics. The comparison revealed. . . pathogens. The standard operational comparison with the most protective, cereal specific emulsion of oil in water displayed that the bacterial ***ghosts*** had equal to or lower efficacy than the emulsion. This study confirmed the potential of bacterial ***ghost*** platform technology as a new alternative carrier system for pesticides.

IT Methods & Equipment
pesticide delivery methods: applied and field techniques

IT Miscellaneous Descriptors
bacterial ***ghost*** technology: applications, descriptions; bacterial ***ghosts*** : pesticide delivery applications, properties; biotechnology; methodologies: applications, descriptions; pest control: methodologies; phytopathology

L2 ANSWER 25 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 18

AN 2004:441247 BIOSIS <<LOGINID::20090617>>

DN PREV200400445959

TI A novel recombinant multisubunit vaccine against Chlamydia.

AU Eko, Francis O. [Reprint Author]; He, Qing; Brown, Teresa; McMillan, Lucinda; Ifere, Godwin O.; Ananaba, Godwin A.; Lyn, Deborah; ***Lubitz,*** *** Werner*** ; Kellar, Kathryn L.; Black, Carolyn M.; Igietseme, Joseph U.

CS Dept Microbiol Biochem and Immunol, Morehouse Sch Med, 720 Westview Dr,SW, Atlanta, GA, 30310, USA
feko@msm.edu

SO Journal of Immunology, (September 1 2004) Vol. 173, No. 5, pp. 3375-3382. print.
ISSN: 0022-1767 (ISSN print).

DT Article

LA English

ED Entered STN: 17 Nov 2004
Last Updated on STN: 17 Nov 2004

AB The administration of an efficacious vaccine is the most effective long-term measure to control the oculogenital infections caused by Chlamydia trachomatis in humans. Chlamydia genome sequencing has identified a number of potential vaccine candidates, and the current challenge is to develop an effective delivery vehicle for induction of a high level of mucosal T and complementary B cell responses. Vibrio cholerae ***ghosts*** (VCG) are nontoxic, effective delivery vehicles with potent adjuvant properties, and are capable of inducing both T cell and Ab responses in mucosal tissues. We investigated the hypothesis that rVCG could serve as effective delivery vehicles for single or multiple subunit chlamydial vaccines to induce a high level of protective immunity. rVCG-expressing chlamydial outer membrane proteins were produced by a two-step genetic process, involving cloning of Omp genes in V. cholerae, followed by gene E-mediated lysis of the cells. The immunogenicity and vaccine efficacy of rVCG-expressing single and multiple subunits were compared. Immunologic analysis indicated that i.m. immunization of mice with either vaccine construct induced a strong mucosal and systemic specific Th1 response against the whole chlamydial organism. However, there was an immunogenic advantage associated with the multiple subunit vaccine that induced a higher frequency of Th1 cells and a relatively greater ability to confer protective immunity, compared with the single

subunit construct. These results support the operational theory that the ability of a vaccine to confer protective immunity against Chlamydia is a function of the level of Th1 response elicited.

AU Eko, Francis O. [Reprint Author]; He, Qing; Brown, Teresa; McMillan, Lucinda; Ifere, Godwin O.; Ananaba, Godwin A.; Lyn, Deborah; ***Lubitz,*** *** Werner*** ; Kellar, Kathryn L.; Black, Carolyn M.; Igietseme, Joseph U.

AB . . an effective delivery vehicle for induction of a high level of mucosal T and complementary B cell responses. Vibrio cholerae ***ghosts*** (VCG) are nontoxic, effective delivery vehicles with potent adjuvant properties, and are capable of inducing both T cell and Ab. . .

IT Methods & Equipment
recombinant Vibrio cholerae ***ghost*** vaccine delivery system: drug delivery device

IT Miscellaneous Descriptors
Th1 response; vaccine development

L2 ANSWER 26 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 19

AN 2004:1089444 CAPLUS <<LOGINID::20090617>>

DN 142:278243

TI Antigen discovery and delivery of subunit vaccines by nonliving bacterial ***ghost*** vectors

AU Walcher, Petra; Mayr, Ulrike B.; Azimpour-Tabrizi, Chakameh; Eko, Francis O.; Jechlinger, Wolfgang; Mayrhofer, Peter; Alefantis, Tim; Mujer, Cesar V.; DelVecchio, Vito G.; ***Lubitz, Werner***

CS Institute of Microbiology and Genetics, Department Microbiology and Biotechnology, University of Vienna, Vienna, A-1090, Austria

SO Expert Review of Vaccines (2004), 3(6), 681-691
CODEN: ERVXAX; ISSN: 1476-0584

PB Future Drugs Ltd.

DT Journal; General Review

LA English

AB A review. The bacterial ***ghost*** (BG) platform system is a novel vaccine delivery system endowed with intrinsic adjuvant properties. BGs are nonliving Gram-neg. bacterial cell envelopes which are devoid of their cytoplasmic contents, yet maintain their cellular morphol. and antigenic structures, including bioadhesive properties. The main advantages of BGs as carriers of subunit vaccines include their ability to stimulate a high immune response and to target the carrier itself to primary antigen-presenting cells. The intrinsic adjuvant properties of BGs enhance the immune response to target antigens, including T-cell activation and mucosal immunity. Since native and foreign antigens can be carried in the envelope complex of BGs, combination vaccines with multiple antigens of diverse origin can be presented to the immune system simultaneously. Beside the capacity of BGs to function as carriers of protein antigens, they also have a high loading capacity for DNA. Thus, loading BGs with recombinant DNA takes advantage of the excellent bioavailability for DNA-based vaccines and the high expression rates of the DNA-encoded antigens in target cell types such as macrophages and dendritic cells. There are many spaces within BGs including the inner and outer membranes, the periplasmic space and the internal lumen which can carry antigens, DNA or mediators of the immune response. All can be used for subunit antigen to design new vaccine candidates with particle presentation technol. In addn., the fact that BGs can also carry piggyback large-size foreign antigen particles, increases the technol.

usefulness of BGs as combination vaccines against viral and bacterial pathogens. Furthermore, the BG antigen carriers can be stored as freeze-dried prepns. at room temp. for extended periods without loss of efficacy. The potency, safety and relatively low prodn. cost of BGs offer a significant tech. advantage over currently utilized vaccine technologies.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Antigen discovery and delivery of subunit vaccines by nonliving bacterial ***ghost*** vectors

AU . . . Mayr, Ulrike B.; Azimpour-Tabrizi, Chakameh; Eko, Francis O.; Jechlinger, Wolfgang; Mayrhofer, Peter; Alefantis, Tim; Mujer, Cesar V.; DelVecchio, Vito G.; ***Lubitz, Werner***

AB A review. The bacterial ***ghost*** (BG) platform system is a novel vaccine delivery system endowed with intrinsic adjuvant properties. BGs are nonliving Gram-neg. bacterial cell. . .

ST review vaccine antigen carrier bacteria ***ghost*** vector

IT Eubacteria
Vaccines
(antigen discovery and delivery of subunit vaccines by nonliving bacterial ***ghost*** vectors)

IT Antigens
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antigen discovery and delivery of subunit vaccines by nonliving bacterial ***ghost*** vectors)

IT Cell envelope
(bacterial; antigen discovery and delivery of subunit vaccines by nonliving bacterial ***ghost*** vectors)

IT Drug delivery systems
(carriers; antigen discovery and delivery of subunit vaccines by nonliving bacterial ***ghost*** vectors)

L2 ANSWER 27 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 20

AN 2005:83975 BIOSIS <<LOGINID::20090617>>

DN PREV200500083911

TI Bacterial ***ghosts*** - biological particles as delivery systems for antigens, nucleic acids and drugs.

AU Tabrizi, Chakameh Azimpour; Walcher, Petra; Mayr, Ulrike Beate; Stiedl, Thomas; Binder, Matthias; McGrath, John; ***Lubitz, Werner*** [Reprint Author]

CS Inst Microbiol and GenetSect Microbiol and Biotechnol, Univ Vienna, Althanstr 14,UZAII,2B 522, A-1090, Vienna, Austria
werner.lubitz@univie.ac.at

SO Current Opinion in Biotechnology, (December 2004) Vol. 15, No. 6, pp. 530-537. print.
ISSN: 0958-1669.

DT Article
General Review; (Literature Review)

LA English

ED Entered STN: 23 Feb 2005
Last Updated on STN: 23 Feb 2005

TI Bacterial ***ghosts*** - biological particles as delivery systems for antigens, nucleic acids and drugs.

AU Tabrizi, Chakameh Azimpour; Walcher, Petra; Mayr, Ulrike Beate; Stiedl, Thomas; Binder, Matthias; McGrath, John; ***Lubitz, Werner*** [Reprint

Author]
IT Methods & Equipment
bacterial ***ghost*** : drug delivery device; vaccination: clinical techniques

L2 ANSWER 28 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 21
AN 2004:1007861 CAPLUS <<LOGINID::20090617>>
DN 142:132586
TI T cell-specific immune response induced by bacterial ***ghosts***
AU Felnerova, Diana; Kudela, Pavel; Bizik, Jozef; Haslberger, Alexander; Hensel, Andreas; Saalmueller, Armin; ***Lubitz, Werner***
CS Institute of Microbiology and Genetics, University of Vienna, Austria
SO Medical Science Monitor (2004), 10(10), BR362-BR370
CODEN: MSMOFR; ISSN: 1234-1010
PB International Scientific Literature, Inc.
DT Journal
LA English
AB Bacterial ***ghosts*** , genetically inactivated Gram-neg. bacterial pathogens, possess significant advantages over commonly used vaccination technologies. The autolysis of the bacteria, by the expression of a cloned viral gene, results in empty bacterial envelopes through the expulsion of cytoplasmic content. Immunostimulatory properties are generally presented via targeting of professional antigen-presenting cells (APCs), such as macrophages and dendritic cells (DCs). This study investigated the interactions between porcine antigen-presenting cells and bacterial ***ghosts*** derived from the bacterial pathogen Actinobacillus pleuropneumoniae. The maturation process of DCs and their generation of immune responses to bacterial ***ghosts*** was shown by the expression of activation markers on their surface, as well as in the functional tests. A population of porcine APCs was generated from PBS by incubation with rpo-GMCSF and rh-IL-4. The cells expressed SWC3, MIL-2, CD80/86 mols., as well as a high level of MSA3 mols. The internalization of bacterial ***ghosts*** by the cells resulted in increased expression of MSA3 mols. The capacity of T cells to proliferate when induced by bacterial ***ghosts*** was 4 times higher in the cultures including APCs than in cultures stimulated with bacterial ***ghosts*** only. The authors found that antigen-presenting cells have the capacity to stimulate specific T cells after the internalization and processing of Actinobacillus ***ghosts*** , as demonstrated by a strong specific T-cell response generated against the ***ghost*** antigens.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI T cell-specific immune response induced by bacterial ***ghosts***
AU Felnerova, Diana; Kudela, Pavel; Bizik, Jozef; Haslberger, Alexander; Hensel, Andreas; Saalmueller, Armin; ***Lubitz, Werner***
AB Bacterial ***ghosts*** , genetically inactivated Gram-neg. bacterial pathogens, possess significant advantages over commonly used vaccination technologies. The autolysis of the bacteria, by the. . . cells (APCs), such as macrophages and dendritic cells (DCs). This study investigated the interactions between porcine antigen-presenting cells and bacterial ***ghosts*** derived from the bacterial pathogen Actinobacillus pleuropneumoniae. The maturation process of DCs and their generation of immune responses to bacterial ***ghosts*** was shown by the expression of activation markers on their surface, as well as in the functional tests. A population. . . The cells expressed SWC3, MIL-2, CD80/86 mols., as well as a high level of MSA3 mols. The internalization of bacterial ***ghosts*** by the cells resulted in increased expression

of MSA3 mols. The capacity of T cells to proliferate when induced by bacterial ***ghosts*** was 4 times higher in the cultures including APCs than in cultures stimulated with bacterial ***ghosts*** only. The authors found that antigen-presenting cells have the capacity to stimulate specific T cells after the internalization and processing of Actinobacillus ***ghosts*** , as demonstrated by a strong specific T-cell response generated against the ***ghost*** antigens.

ST T cell immunostimulation bacterial ***ghost*** vaccine

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MSA3; dendritic cell-mediated T cell-specific immune response in pigs induction by bacterial ***ghosts*** as veterinary vaccine in relation to expression of)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SLA-DR; dendritic cell-mediated T cell-specific immune response in pigs induction by bacterial ***ghosts*** as veterinary vaccine in relation to expression of)

IT Immunostimulation
(cellular; dendritic cell-mediated T cell-specific immune response in pigs induction by bacterial ***ghosts*** as veterinary vaccine)

IT Actinobacillus pleuropneumoniae
Antigen-presenting cell
Dendritic cell
Gram-negative bacteria
Sus scrofa domestica
T cell (lymphocyte)
(dendritic cell-mediated T cell-specific immune response in pigs induction by bacterial ***ghosts*** as veterinary vaccine)

IT Vaccines
(veterinary; dendritic cell-mediated T cell-specific immune response in pigs induction by bacterial ***ghosts*** as veterinary vaccine)

L2 ANSWER 29 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 22

AN 2005:554493 BIOSIS <<LOGINID::20090617>>

DN PREV200510341926

TI Minicircle DNA immobilized in bacterial ***ghosts*** : In vivo production of safe non-viral DNA delivery vehicles.

AU Jechlinger, Wolfgang [Reprint Author]; Azimpour Tabrizi, Chakameh; ***Lubitz, Werner*** ; Mayrhofer, Peter

CS Univ Vet Med, Dept Pathobiol, Inst Bacteriol Mycol and Hyg, Vet Pl 1, A-1210 Vienna, Austria
Wolfgang.Jechlinger@vu-wien.ac.at

SO Journal of Molecular Microbiology and Biotechnology, (2004) Vol. 8, No. 4, pp. 222-231.
ISSN: 1464-1801.

DT Article

LA English

ED Entered STN: 7 Dec 2005
Last Updated on STN: 7 Dec 2005

AB DNA as an active agent is among the most promising technologies for vaccination and therapy. However, plasmid backbone sequences needed for the production of pDNA in bacteria are dispensable, reduce the efficiency of the DNA agent and, most importantly, represent a biological safety risk. In this report we describe a novel technique where a site-specific recombination system based on the ParA resolvase was applied to a

self-immobilizing plasmid system (SIP). In addition, this system was combined with the protein E-specific lysis technology to produce non-living bacterial carrier vehicles loaded with minicircle DNA. The in vivo recombination process completely divided an origin plasmid into a minicircle and a miniplasmid. The replicative miniplasmid containing the origin of replication and the antibiotic resistance gene was lost during the subsequently induced PhiX174 gene E - mediated lysis process, which results in bacterial ***ghosts*** . The minicircle DNA was retained in these empty bacterial cell envelopes during the lysis process via the specific interaction of a membrane anchored protein with the minicircle DNA. Using this novel platform technology, a DNA delivery vehicle - consisting of a safe bacterial carrier with known adjuvant properties and minicircle DNA with an optimized safety profile - can be produced in vivo in a continuous process. Furthermore, this study provides the basis for the development of an efficient in vitro minicircle purification process. Copyright (C) 2004 S. Karger AG, Basel.

TI Minicircle DNA immobilized in bacterial ***ghosts*** : In vivo production of safe non-viral DNA delivery vehicles.

AU Jechlinger, Wolfgang [Reprint Author]; Azimpour Tabrizi, Chakameh; ***Lubitz, Werner*** ; Mayrhofer, Peter

AB. . . antibiotic resistance gene was lost during the subsequently induced PhiX174 gene E - mediated lysis process, which results in bacterial ***ghosts*** . The minicircle DNA was retained in these empty bacterial cell envelopes during the lysis process via the specific interaction of. . .

IT Methods & Equipment
vaccination: clinical techniques; DNA delivery vehicle: drug delivery device

IT Miscellaneous Descriptors
bacterial ***ghost***

L2 ANSWER 30 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 23

AN 2004:218708 BIOSIS <<LOGINID::20090617>>

DN PREV200400218362

TI Bacterial ***ghosts*** as novel advanced drug delivery systems: Antiproliferative activity of loaded doxorubicin in human Caco-2 cells.

AU Paukner, Susanne [Reprint Author]; Kohl, Gudrun; ***Lubitz, Werner***

CS BIRD-C GmbH and Co KEG, Schonborngasse 12/12, 1080, Wien, Austria

SO Journal of Controlled Release, (8 January 2004) Vol. 94, No. 1, pp. 63-74. print.
ISSN: 0168-3659 (ISSN print).

DT Article

LA English

ED Entered STN: 21 Apr 2004
Last Updated on STN: 21 Apr 2004

AB Systemic application of anticancer drugs often causes severe toxic side effects. To reduce the undesired effects, advanced drug delivery systems are needed which are based on specific cell targeting vehicles. In this study, bacterial ***ghosts*** from Mannheimia haemolytica were used for site-specific delivery of doxorubicin (DOX) to human colorectal adenocarcinoma cells (Caco-2). Bacterial ***ghosts*** are non-denatured envelopes of Gram-negative bacteria with fully intact surface structures for specific attachment to mammalian cells. The in vitro release profile of DOX- ***ghosts*** demonstrated that the loaded drug was non-covalently associated with the bacterial ***ghosts*** and that the drug delivery vehicles themselves represent a slow release

system. Adherence studies showed that the M. haemolytica ***ghosts*** more efficiently than E. coli ***ghosts*** targeted the Caco-2 cells and released the loaded DOX within the cells. Cytotoxicity assays revealed that the DOX- ***ghosts*** exhibited potent antiproliferative activities on Caco-2 cells as the DOX associated with ***ghosts*** was two magnitude of orders more cytotoxic than free DOX provided in the medium at the same concentrations. Notably, a significant reduction in the cell viability was measured with DOX- ***ghosts*** at low DOX concentrations, which had no inhibitory effect when applied as free DOX after incubation for 16 h or when applied at higher concentrations for only 10 min to the cells. As the higher antiproliferative effects of DOX on Caco-2 cells were mediated by the specific drug targeting properties of the bacterial ***ghosts*** , the bacterial ***ghost*** system represents a novel platform for advanced drug delivery.

TI Bacterial ***ghosts*** as novel advanced drug delivery systems: Antiproliferative activity of loaded doxorubicin in human Caco-2 cells.

AU Paukner, Susanne [Reprint Author]; Kohl, Gudrun; ***Lubitz, Werner***

AB. . . undesired effects, advanced drug delivery systems are needed which are based on specific cell targeting vehicles. In this study, bacterial ***ghosts*** from Mannheimia haemolytica were used for site-specific delivery of doxorubicin (DOX) to human colorectal adenocarcinoma cells (Caco-2). Bacterial ***ghosts*** are non-denatured envelopes of Gram-negative bacteria with fully intact surface structures for specific attachment to mammalian cells. The in vitro release profile of DOX- ***ghosts*** demonstrated that the loaded drug was non-covalently associated with the bacterial ***ghosts*** and that the drug delivery vehicles themselves represent a slow release system. Adherence studies showed that the M. haemolytica ***ghosts*** more efficiently than E. coli ***ghosts*** targeted the Caco-2 cells and released the loaded DOX within the cells. Cytotoxicity assays revealed that the DOX- ***ghosts*** exhibited potent antiproliferative activities on Caco-2 cells as the DOX associated with ***ghosts*** was two magnitude of orders more cytotoxic than free DOX provided in the medium at the same concentrations. Notably, a significant reduction in the cell viability was measured with DOX- ***ghosts*** at low DOX concentrations, which had no inhibitory effect when applied as free DOX after incubation for 16 h or. . . the higher antiproliferative effects of DOX on Caco-2 cells were mediated by the specific drug targeting properties of the bacterial ***ghosts*** , the bacterial ***ghost*** system represents a novel platform for advanced drug delivery.

ORGN . . .
Vertebrates

ORGN Classifier
Pasteurellaceae 06703

Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms

Organism Name
Mannheimia haemolytica (species): bacterial ***ghost***

Taxa Notes
Bacteria, Eubacteria, Microorganisms

L2 ANSWER 31 OF 54 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

AN 2004459102 EMBASE <<LOGINID::20090617>>

TI T cell-specific immune response induced by bacterial ***ghosts*** .

AU Felnerova, Diana (correspondence); Haslberger, Alexander; ***Lubitz,***

Werner
CS Inst. of Microbiology and Genetics, University of Vienna, Austria. diana.felnerova@bernabiotech.com
AU Felnerova, Diana (correspondence); Kudela, Pavel; Bizik, Jozef
CS Cancer Research Institute, Slovak Academy of Sciences, Bratislava, Slovakia. diana.felnerova@bernabiotech.com
AU Hensel, Andreas
CS Inst. of Anim. Hyg./Vet. Pub. Hlth., University of Leipzig, Germany.
AU Saalmuller, Armin
CS Fed. Res. Ctr. Virus Dis. of Animals, Institute of Immunology, Tubingen, Germany.
AU Felnerova, Diana (correspondence)
CS Berna Biotech Ltd., Vaccine Research, Berne, Switzerland. diana.felnerova@bernabiotech.com
SO Medical Science Monitor, (Oct 2004) Vol. 10, No. 10, pp. BR362-BR370.
Refs: 21
ISSN: 1234-1010 CODEN: MSMOFR
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 19 Nov 2004
Last Updated on STN: 19 Nov 2004
AB Background: Bacterial ***ghosts*** , genetically inactivated Gram-negative bacterial pathogens, possess significant advantages over commonly used vaccination technologies. The autolysis of the bacteria, by the expression of a cloned viral gene, results in empty bacterial envelopes through the expulsion of cytoplasmic content. Immunostimulatory properties are generally presented through the targeting of professional antigen-presenting cells (APCs), such as macrophages and dendritic cells (DCs). Material/Methods: This study investigated the interactions between porcine antigen-presenting cells and bacterial ***ghosts*** derived from the bacterial pathogen Actinobacillus pleuropneumoniae. The maturation process of DCs and their generation of immune responses to bacterial ***ghosts*** was shown by the expression of activation markers on their surface, as well as in the functional tests. Results: A population of porcine APCs was generated from PBS by incubation with rpo-GMCSF and rh-IL-4. The cells expressed SWC3, MIL-2, CD80/86 molecules, as well as a high level of MSA3 molecules. The internalization of bacterial ***ghosts*** by the cells resulted in increased expression of MSA3 molecules. The capacity of T cells to proliferate when induced by bacterial ***ghosts*** was 4 times higher in the cultures including APCs than in cultures stimulated with bacterial ***ghosts*** only. Conclusions: We found that antigen-presenting cells have the capacity to stimulate specific T cells after the internalization and processing of Actinobacillus ***ghosts*** , as demonstrated by a strong specific T-cell response generated against the ***ghost*** antigens.
TI T cell-specific immune response induced by bacterial ***ghosts*** .
AU Felnerova, Diana (correspondence); Haslberger, Alexander; ***Lubitz,*** ***Werner***
CS Inst. of Microbiology and Genetics, University of Vienna, Austria. diana.felnerova@bernabiotech.com
AB Background: Bacterial ***ghosts*** , genetically inactivated Gram-negative bacterial pathogens, possess significant advantages over commonly used vaccination technologies. The autolysis of the bacteria, by

the. . . (APCs), such as macrophages and dendritic cells (DCs). Material/Methods: This study investigated the interactions between porcine antigen-presenting cells and bacterial ***ghosts*** derived from the bacterial pathogen Actinobacillus pleuropneumoniae. The maturation process of DCs and their generation of immune responses to bacterial ***ghosts*** was shown by the expression of activation markers on their surface, as well as in the functional tests. Results: A. . . The cells expressed SWC3, MIL-2, CD80/86 molecules, as well as a high level of MSA3 molecules. The internalization of bacterial ***ghosts*** by the cells resulted in increased expression of MSA3 molecules. The capacity of T cells to proliferate when induced by bacterial ***ghosts*** was 4 times higher in the cultures including APCs than in cultures stimulated with bacterial ***ghosts*** only. Conclusions: We found that antigen-presenting cells have the capacity to stimulate specific T cells after the internalization and processing of Actinobacillus ***ghosts*** , as demonstrated by a strong specific T-cell response generated against the ***ghost*** antigens.

CT Medical Descriptors:
Actinobacillus pleuropneumoniae
animal cell
antigen presenting cell
*antigen specificity
article
autolysis
****bacterial ghost***
bacterial membrane
cellular immunity
dendritic cell
gene inactivation
Gram negative bacterium
*immune response
internalization
nonhuman
swine
*T lymphocyte activation
vaccination
veterinary medicine
virus gene
vaccine

L2 ANSWER 32 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2003:58229 CAPLUS <<LOGINID::20090617>>
DN 138:112418
TI Nucleic acid free bacterial ***ghost*** preparations for drug delivery
IN ***Lubitz, Werner*** ; Haidinger, Wolfgang
PA Apovia A.-G., Germany
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006630	A2	20030123	WO 2002-EP7758	20020711
	WO 2003006630	A3	20031023		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA	2453518	A1	20030123	CA 2002-2453518	20020711
AU	2002328340	A1	20030129	AU 2002-328340	20020711
AU	2002328340	B2	20070628		
EP	1404808	A2	20040407	EP 2002-762349	20020711
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
NZ	530780	A	20050624	NZ 2002-530780	20020711
US	20040213810	A1	20041028	US 2004-483595	20040112
US	7399476	B2	20080715		
PRAI US	2001-304595P	P	20010711		
WO	2002-EP7758	W	20020711		

AB The invention relates to prepns. of bacterial ***ghosts*** which are substantially free of living bacterial cells and/or nucleic acids and their use in pharmaceutical prepns.

TI Nucleic acid free bacterial ***ghost*** preparations for drug delivery

IN ***Lubitz, Werner*** ; Haidinger, Wolfgang

AB The invention relates to prepns. of bacterial ***ghosts*** which are substantially free of living bacterial cells and/or nucleic acids and their use in pharmaceutical prepns.

ST bacteria ***ghost*** prepn drug delivery

IT Immunostimulants
(adjuvants; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Drug delivery systems
(carriers; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cell-lytic; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Eubacteria
(***ghosts*** ; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lytic protein-encoding; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lytic, genes encoding; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Staphylococcus aureus
(nuclease gene of; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

IT Coliphage .phi.X174
Cytolysis
Drug delivery systems
Human

Vaccines
(nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)
IT Nucleic acids
RL: REM (Removal or disposal); PROC (Process)
(nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)
IT 9026-81-7, Nuclease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene encoding; nucleic acid-free bacterial ***ghost*** prepns. for drug delivery)

L2 ANSWER 33 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 24
AN 2003:457999 BIOSIS <<LOGINID::20090617>>
DN PREV200300457999
TI Evaluation of the protective efficacy of Vibrio cholerae ***ghost*** (VCG) candidate vaccines in rabbits.
AU Eko, Francis O. [Reprint Author]; Schukovskaya, Tatiana; Lotzmanova, E. Y.; Firstova, V. V.; Emalyanova, N. V.; Klueva, S. N.; Kravtzov, A. L.; Livanova, L. F.; Kutyrev, Vladimir V.; Igietseme, Joseph U.; ***Lubitz, *** *** Werner***
CS Department of Microbiology, Biochemistry and Immunology, Morehouse School of Medicine, 720 Westview Dr., S. W. Atlanta, GA, 30310, USA
feko@msm.edu
SO Vaccine, (8 September 2003) Vol. 21, No. 25-26, pp. 3663-3674. print.
ISSN: 0264-410X (ISSN print).
DT Article
LA English
ED Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003
AB An effective Vibrio cholerae vaccine is needed to reduce the morbidity and mortality caused by this pathogen. Despite the availability of current oral vaccines with measurable efficacy, there is need for more effective vaccines with broad-spectrum efficacy in target populations. Recent studies have shown that bacterial ***ghosts*** , produced by the expression of cloned lysis gene E, possess adjuvant properties and are immunogenic. In this study, ***ghosts*** were prepared from V. cholerae 01 or 0139 and evaluated as vaccines in the reversible intestinal tie adult rabbit diarrhea (RITARD) model. Rabbits were orally immunized with different doses of V. cholerae ***ghost*** (VCG) formulations. The vaccine formulations elicited high levels of serum vibriocidal titers against indicator strains. The magnitude of the response was measured as the geometric mean titer (GMT) increase for all rabbits in relation to prevaccination titers. The induction of cross protection was evidenced by the ability of serum from VCG-immunized rabbits to mediate complement-dependent killing of both the homologous and the heterologous strains. Immunized rabbits were protected against intraduodenal challenge 30 days after primary immunization. Protective immunity against challenge appeared to be dose dependent and was associated with marked inhibition of colonization. These results indicate that VCGs represent a novel approach to cholera vaccine development and constitute an effective vaccine delivery vehicle.
TI Evaluation of the protective efficacy of Vibrio cholerae ***ghost*** (VCG) candidate vaccines in rabbits.
AU. . . V. V.; Emalyanova, N. V.; Klueva, S. N.; Kravtzov, A. L.; Livanova, L. F.; Kutyrev, Vladimir V.; Igietseme, Joseph U.; ***Lubitz, Werner***
AB. . . efficacy, there is need for more effective vaccines with

broad-spectrum efficacy in target populations. Recent studies have shown that bacterial ***ghosts*** , produced by the expression of cloned lysis gene E, possess adjuvant properties and are immunogenic. In this study, ***ghosts*** were prepared from V. cholerae 01 or 0139 and evaluated as vaccines in the reversible intestinal tie adult rabbit diarrhea (RITARD) model. Rabbits were orally immunized with different doses of V. cholerae ***ghost*** (VCG) formulations. The vaccine formulations elicited high levels of serum vibriocidal titers against indicator strains. The magnitude of the response. . .

IT . . .
lymphatics

IT Diseases
cholera: bacterial disease
Cholera (MeSH)

IT Diseases
diarrhea: digestive system disease
Diarrhea (MeSH)

IT Chemicals & Biochemicals
Vibrio cholerae ***ghost*** candidate vaccine: immunologic-drug, immunostimulant-drug, vaccine

L2 ANSWER 34 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 25

AN 2003:207111 BIOSIS <<LOGINID::20090617>>

DN PREV200300207111

TI Recombinant Vibrio cholerae ***ghosts*** as a delivery vehicle for vaccinating against Chlamydia trachomatis.

AU Eko, Francis O. [Reprint Author]; ***Lubitz, Werner*** ; McMillan, Lucinda; Ramey, Kiantra; Moore, Terri T.; Ananaba, Godwin A.; Lyn, Deborah; Black, Carolyn M.; Igietseme, Joseph U.

CS Department of Microbiology, Biochemistry and Immunology, Morehouse School of Medicine, 720 Westview Dr. SW, Atlanta, GA, 30310, USA
feko@msm.edu

SO Vaccine, (2 April 2003) Vol. 21, No. 15, pp. 1694-1703. print.
ISSN: 0264-410X (ISSN print).

DT Article

LA English

ED Entered STN: 30 Apr 2003
Last Updated on STN: 30 Apr 2003

AB An efficacious vaccine is needed to control the morbidity and burden of rising healthcare costs associated with genital Chlamydia trachomatis infection. Despite considerable efforts, the development of reliable chlamydial vaccines using conventional strategies has proven to be elusive. The 40 kDa major outer membrane protein (MOMP) of C. trachomatis is so far the most promising candidate for a subunit vaccine. The lack of satisfactory protective immunity with MOMP-based vaccine regimens to date would suggest that either MOMP alone is inadequate as a vaccine candidate or better delivery systems are needed to optimize the effect of MOMP. Recombinant Vibrio cholerae ***ghosts*** (rVCG) are attractive for use as non-living vaccines because they possess strong adjuvant properties and are excellent vehicles for delivery of antigens of vaccine relevance to mucosal sites. The suitability of the ***ghost*** technology for designing an anti-chlamydial vaccine was evaluated by constructing a rVCG vector-based candidate vaccine expressing MOMP (rVCG-MOMP) and assessing vaccine efficacy in a murine model of C. trachomatis genital infection. Intramuscular delivery of the rVCG-MOMP vaccine induced elevated local genital mucosal as well as systemic Th1 responses. In addition, immune T

cells from immunized mice could transfer partial protection against a C. trachomatis genital challenge to naive mice. These results suggest that rVCG expressing chlamydial proteins may constitute a suitable subunit vaccine for inducing an efficient mucosal T cell response that protects against C. trachomatis infection. Altogether, the potency and relatively low production cost of rVCG offer a significant technical advantage as a chlamydial vaccine.

TI Recombinant Vibrio cholerae ***ghosts*** as a delivery vehicle for vaccinating against Chlamydia trachomatis.

AU Eko, Francis O. [Reprint Author]; ***Lubitz, Werner*** ; McMillan, Lucinda; Ramey, Kiantra; Moore, Terri T.; Ananaba, Godwin A.; Lyn, Deborah; Black, Carolyn M.; Igietseme, Joseph U.

AB. . . inadequate as a vaccine candidate or better delivery systems are needed to optimize the effect of MOMP. Recombinant Vibrio cholerae ***ghosts*** (rVCG) are attractive for use as non-living vaccines because they possess strong adjuvant properties and are excellent vehicles for delivery of antigens of vaccine relevance to mucosal sites. The suitability of the ***ghost*** technology for designing an anti-chlamydial vaccine was evaluated by constructing a rVCG vector-based candidate vaccine expressing MOMP (rVCG-MOMP) and assessing. . .

IT . . .

IT Chemicals & Biochemicals
anti-chlamydial vaccine: efficacy, intramuscular administration, vaccine; chlamydial proteins; major outer membrane protein [MOMP]; recombinant Vibrio cholerae ***ghosts*** -major outer membrane protein vaccine [rVOG-MOMP vaccine]: vaccine; subunit vaccine: vaccine

ORGN . . .
06704
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Vibrio cholerae (species): gene vector, delivery vehicle, recombinant ***ghosts*** , strain-HM12
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L2 ANSWER 35 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 26

AN 2003:439696 BIOSIS <<LOGINID::20090617>>

DN PREV200300439696

TI Construction of recombinant S-layer proteins (rSbsA) and their expression in bacterial ***ghosts*** : A delivery system for the nontypeable Haemophilus influenzae antigen Omp26.

AU Riedmann, Eva M. [Reprint Author]; Kyd, Jennelle M.; Smith, Adam M.; Gomez-Gallego, Sara; Jalava, Katri; Cripps, Allan W.; ***Lubitz,*** ***Werner***

CS Institute of Microbiology and Genetics, University of Vienna, Vienna Biocentre, 1090, Vienna, Austria
eva.riedmann@univie.ac.at

SO FEMS Immunology and Medical Microbiology, (15 July 2003) Vol. 37, No. 2-3, pp. 185-192. print.
ISSN: 0928-8244 (ISSN print).

DT Article

LA English

ED Entered STN: 24 Sep 2003
Last Updated on STN: 24 Sep 2003

AB This study has investigated the feasibility of a combination of recombinant surface layer (S-layer) proteins and empty bacterial cell envelopes (***ghosts***) to deliver candidate antigens for a vaccine against nontypeable Haemophilus influenzae (NTHi) infections. The S-layer gene sbsA from Bacillus stearothermophilus PV72 was used for the construction of fusion proteins. Fusion of maltose binding protein (MBP) to the N-terminus of SbsA allowed expression of the S-layer in the periplasm of Escherichia coli. The outer membrane protein (Omp) 26 of NTHi was inserted into the N-terminal and C-terminal regions of SbsA. The presence of the fused antigen Omp26 was demonstrated by Western blot experiments using anti-Omp26 antisera. Electron microscopy showed that the recombinant SbsA maintained the ability to self-assemble into sheet-like and cylindrical structures. Recombinant E. coli cell envelopes (***ghosts***) were produced by the expression of SbsA/Omp26 fusion proteins prior to gene E-mediated lysis. Intraperitoneal immunization with these recombinant bacterial ***ghosts*** induced an Omp26-specific antibody response in BALB/c mice. These results demonstrate that the NTHi antigen, Omp26, was expressed in the S-layer self-assembly product and this construct was immunogenic for Omp26 when administered to mice in bacterial cell envelopes.

TI Construction of recombinant S-layer proteins (rSbsA) and their expression in bacterial ***ghosts*** : A delivery system for the nontypeable Haemophilus influenzae antigen Omp26.

AU Riedmann, Eva M. [Reprint Author]; Kyd, Jennelle M.; Smith, Adam M.; Gomez-Gallego, Sara; Jalava, Katri; Cripps, Allan W.; ***Lubitz,*** ***Werner***

AB. . . This study has investigated the feasibility of a combination of recombinant surface layer (S-layer) proteins and empty bacterial cell envelopes (***ghosts***) to deliver candidate antigens for a vaccine against nontypeable Haemophilus influenzae (NTHi) infections. The S-layer gene sbsA from Bacillus stearothermophilus. . . showed that the recombinant SbsA maintained the ability to self-assemble into sheet-like and cylindrical structures. Recombinant E. coli cell envelopes (***ghosts***) were produced by the expression of SbsA/Omp26 fusion proteins prior to gene E-mediated lysis. Intraperitoneal immunization with these recombinant bacterial ***ghosts*** induced an Omp26-specific antibody response in BALB/c mice. These results demonstrate that the NTHi antigen, Omp26, was expressed in the. . .

IT . . .
recombinant, surface layer protein; SbsA-Omp26 fusion protein: immunologic-drug, immunostimulant-drug; nontypeable Haemophilus influenzae infection vaccine: immunologic-drug, immunostimulant-drug, pharmacodynamics; recombinant S-layer protein-bacterial ***ghost*** combination [rSbsA-bacterial ***ghost*** combination]: immunologic-drug, immunostimulant-drug, construction, expression

L2 ANSWER 36 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 27

AN 2003:575434 BIOSIS <<LOGINID::20090617>>

DN PREV200300580932

TI Sealed bacterial ***ghosts*** : Novel targeting vehicles for advanced drug delivery of water-soluble substances.

AU Paukner, Susanne [Reprint Author]; Kohl, Gudrun; Jalava, Katri; ***Lubitz, Werner***

CS Institute for Microbiology and Genetics, University Vienna, Althanstrasse14, Vienna Biocenter, 1090, Vienna, Austria susanne.paukner@univie.ac.at

SO Journal of Drug Targeting, (April 2003) Vol. 11, No. 3, pp. 151-161. print.
ISSN: 1061-186X (ISSN print).
DT Article
LA English
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB The purpose of the present study was to develop a drug delivery model for water soluble drug substances using the bacterial ***ghost*** platform technology. Bacterial ***ghosts*** are non-denatured bacterial cell envelopes that are produced by the plasmid encoded gene E mediated lysis. We present a novel method to fill and seal bacterial ***ghosts*** for the application as a drug delivery system for fluid, non-anchored substances. E. coli ***ghosts*** were filled with the reporter substance calcein and sealed by fusion with membrane vesicles. By flow cytometry and fluorescence microscopy it was shown that bacterial ***ghosts*** can be filled with calcein, and that the bacterial ***ghosts*** can be sealed by restoring the membranes integrity. The adherence and uptake studies showed that almost all murine macrophages and a lower proportion of human colorectal adenocarcinoma cells took up fluorescence labeled bacterial ***ghosts*** . Moreover, these cells also took up effectively sealed E. coli ***ghosts*** filled with calcein, which then was released within the cells. Therefore, we propose bacterial ***ghosts*** as alternative drug delivery and release vehicles for advanced cell targeting.
TI Sealed bacterial ***ghosts*** : Novel targeting vehicles for advanced drug delivery of water-soluble substances.
AU Paukner, Susanne [Reprint Author]; Kohl, Gudrun; Jalava, Katri; ***Lubitz, Werner***
AB. . . purpose of the present study was to develop a drug delivery model for water soluble drug substances using the bacterial ***ghost*** platform technology. Bacterial ***ghosts*** are non-denatured bacterial cell envelopes that are produced by the plasmid encoded gene E mediated lysis. We present a novel method to fill and seal bacterial ***ghosts*** for the application as a drug delivery system for fluid, non-anchored substances. E. coli ***ghosts*** were filled with the reporter substance calcein and sealed by fusion with membrane vesicles. By flow cytometry and fluorescence microscopy it was shown that bacterial ***ghosts*** can be filled with calcein, and that the bacterial ***ghosts*** can be sealed by restoring the membranes integrity. The adherence and uptake studies showed that almost all murine macrophages and a lower proportion of human colorectal adenocarcinoma cells took up fluorescence labeled bacterial ***ghosts*** . Moreover, these cells also took up effectively sealed E. coli ***ghosts*** filled with calcein, which then was released within the cells. Therefore, we propose bacterial ***ghosts*** as alternative drug delivery and release vehicles for advanced cell targeting.
IT Major Concepts
Membranes (Cell Biology); Pharmaceuticals (Pharmacology)
IT Parts, Structures, & Systems of Organisms
bacterial ***ghosts***

L2 ANSWER 37 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 28
AN 2003:94702 BIOSIS <<LOGINID::20090617>>
DN PREV200300094702
TI Generation of Helicobacter pylori ***ghosts*** by PhiX protein

E-mediated inactivation and their evaluation as vaccine candidates.
AU Panthel, Klaus; Jechlinger, Wolfgang; Matis, Alexander; Rohde, Manfred; Szostak, Michael; ***Lubitz, Werner*** ; Haas, Rainer [Reprint Author]
CS Max von Pettenkofer-Institute for Hygiene and Medical Microbiology, Pettenkoferstr. 9a, D-80336, Munich, Germany
haas@m3401.mpk.med.uni-muenchen.de
SO Infection and Immunity, (January 2003) Vol. 71, No. 1, pp. 109-116. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 12 Feb 2003
Last Updated on STN: 12 Feb 2003
AB Bacterial ***ghosts*** are empty cell envelopes, which may be generated by the controlled expression of the PhiX174 lysis gene E in gram-negative bacteria to obtain vaccine candidates. We describe here the application of this technology to Helicobacter pylori. The lysis gene cassette was cloned into an Escherichia coli-Helicobacter pylori shuttle vector and introduced into an H. pylori recipient strain by bacterial conjugation. Temperature induction of the lysis gene cassette revealed a quantitative killing of the H. pylori culture without induction of lysis-resistant bacteria. Biochemical and transmission electron microscopic studies identified structurally intact H. pylori. Prophylactic oral vaccination experiments using these H. pylori ***ghosts*** in the BALB/c mouse model showed a significant reduction of the bacterial load in the ***ghost*** group, as measured by a quantitative bacterial reisolation procedure. Ten of 10 and 5 of 10 mice were protected, respectively, without the use of a mucosal adjuvant. Coadministration of ***ghosts*** with cholera toxin as mucosal adjuvant resulted in a complete protection of 10 of 10 and 8 of 8 mice against H. pylori challenge, with three animals showing a sterile immunity.
TI Generation of Helicobacter pylori ***ghosts*** by PhiX protein
E-mediated inactivation and their evaluation as vaccine candidates.
AU Panthel, Klaus; Jechlinger, Wolfgang; Matis, Alexander; Rohde, Manfred; Szostak, Michael; ***Lubitz, Werner*** ; Haas, Rainer [Reprint Author]
AB Bacterial ***ghosts*** are empty cell envelopes, which may be generated by the controlled expression of the PhiX174 lysis gene E in gram-negative. . . bacteria. Biochemical and transmission electron microscopic studies identified structurally intact H. pylori. Prophylactic oral vaccination experiments using these H. pylori ***ghosts*** in the BALB/c mouse model showed a significant reduction of the bacterial load in the ***ghost*** group, as measured by a quantitative bacterial reisolation procedure. Ten of 10 and 5 of 10 mice were protected, respectively, without the use of a mucosal adjuvant. Coadministration of ***ghosts*** with cholera toxin as mucosal adjuvant resulted in a complete protection of 10 of 10 and 8 of 8 mice. . .
IT . . .
clinical techniques, therapeutic and prophylactic techniques; transmission electron microscopy: imaging and microscopy techniques, laboratory techniques
IT Miscellaneous Descriptors
Helicobacter pylori ***ghosts*** : generation; PhiX protein E-mediated inactivation; bacterial ***ghosts*** : empty cell envelopes; bacterial load; sterile immunity; vaccine candidates

L2 ANSWER 38 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 29
AN 2003:152097 CAPLUS <<LOGINID::20090617>>
DN 139:250032
TI Bacterial ***ghosts*** as carrier and targeting systems for mucosal antigen delivery
AU Jalava, Katri; Eko, Francis O.; Riedmann, Eva; ***Lubitz, Werner***
CS BIRD-C GmbH & CoKEG, Vienna, A-1080, Austria
SO Expert Review of Vaccines (2003), 2(1), 45-51
CODEN: ERVXAX; ISSN: 1476-0584
PB Future Drugs Ltd.
DT Journal; General Review
LA English
AB A review. The application of new strategies to develop effective vaccines is essential in modern medicine. The bacterial ***ghost*** system is a novel vaccine delivery system endowed with intrinsic adjuvant properties. Bacterial ***ghosts*** are nonliving Gram-neg. bacterial cell envelopes devoid of cytoplasmic contents while maintaining their cellular morphol. and native surface antigenic structures including bioadhesive properties. They are produced by PhiX174 protein E-mediated lysis of Gram-neg. bacteria. The intrinsic adjuvant properties of bacterial ***ghost*** prepns. enhance immune responses against envelope-bound antigens, including T-cell activation and mucosal immunity. Since native and foreign antigens can be expressed in the envelope complex of ***ghosts*** before E-mediated lysis, multiple antigens of various origin can be presented to the immune system simultaneously. In addn., the extended bacterial ***ghost*** system represents a platform technol. for specific targeting of DNA-encoded antigens to primary antigen-presenting cells. The potency, safety and relatively low prodn. cost of bacterial ***ghosts*** offer a significant tech. advantage, esp. when used as combination vaccines.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Bacterial ***ghosts*** as carrier and targeting systems for mucosal antigen delivery
AU Jalava, Katri; Eko, Francis O.; Riedmann, Eva; ***Lubitz, Werner***
AB A review. The application of new strategies to develop effective vaccines is essential in modern medicine. The bacterial ***ghost*** system is a novel vaccine delivery system endowed with intrinsic adjuvant properties. Bacterial ***ghosts*** are nonliving Gram-neg. bacterial cell envelopes devoid of cytoplasmic contents while maintaining their cellular morphol. and native surface antigenic structures. . . including bioadhesive properties. They are produced by PhiX174 protein E-mediated lysis of Gram-neg. bacteria. The intrinsic adjuvant properties of bacterial ***ghost*** prepns. enhance immune responses against envelope-bound antigens, including T-cell activation and mucosal immunity. Since native and foreign antigens can be expressed in the envelope complex of ***ghosts*** before E-mediated lysis, multiple antigens of various origin can be presented to the immune system simultaneously. In addn., the extended bacterial ***ghost*** system represents a platform technol. for specific targeting of DNA-encoded antigens to primary antigen-presenting cells. The potency, safety and relatively low prodn. cost of bacterial ***ghosts*** offer a significant tech. advantage, esp. when used as combination vaccines.
IT Immunostimulants
(adjuvants; bacterial ***ghosts*** as carrier and targeting systems for mucosal antigen delivery)

IT Antigen-presenting cell
Eubacteria
Mucous membrane
Vaccines
(bacterial ***ghosts*** as carrier and targeting systems for mucosal antigen delivery)

L2 ANSWER 39 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 30
AN 2003:101955 BIOSIS <<LOGINID::20090617>>
DN PREV200300101955
TI Bacterial ***ghosts*** as vaccine candidates for veterinary applications.
AU Jalava, Katri [Reprint Author]; Hensel, Andreas; Szostak, Michael; Resch, Stephanie; ***Lubitz, Werner***
CS Biotech Innovation Research Development and Consulting (BIRD-C GmbH and CoKEG), Schoenborngasse 12, A-1080, Vienna, Austria
jalava@bird-c.com
SO Journal of Controlled Release, (13 December 2002) Vol. 85, No. 1-3, pp. 17-25. print.
ISSN: 0168-3659 (ISSN print).
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 19 Feb 2003
Last Updated on STN: 19 Feb 2003
AB The application of new strategies to develop effective vaccines is essential in modern veterinary medicine. The bacterial ***ghost*** system is a novel vaccine delivery system endowed with intrinsic adjuvant properties. Bacterial ***ghosts*** are nonliving Gram-negative bacterial cell envelopes devoid of cytoplasmic contents while maintaining their cellular morphology and native surface antigenic structures including bioadhesive properties. They are produced by PhiX174 protein E-mediated lysis of Gram-negative bacteria. The intrinsic adjuvant properties of bacterial ***ghost*** preparations enhance immune responses against envelope bound antigens, including T-cell activation and mucosal immunity. Since native and foreign antigens can be expressed in the envelope complex of ***ghosts*** before E-mediated lysis, multiple antigens of various origins can be presented to the immune system simultaneously. The advantages of bacterial ***ghosts*** include the simplicity of the production method, safety, independence from the cold chain, and versatility as a combination vaccine.
TI Bacterial ***ghosts*** as vaccine candidates for veterinary applications.
AU Jalava, Katri [Reprint Author]; Hensel, Andreas; Szostak, Michael; Resch, Stephanie; ***Lubitz, Werner***
AB The application of new strategies to develop effective vaccines is essential in modern veterinary medicine. The bacterial ***ghost*** system is a novel vaccine delivery system endowed with intrinsic adjuvant properties. Bacterial ***ghosts*** are nonliving Gram-negative bacterial cell envelopes devoid of cytoplasmic contents while maintaining their cellular morphology and native surface antigenic structures. . . including bioadhesive properties. They are produced by PhiX174 protein E-mediated lysis of Gram-negative bacteria. The intrinsic adjuvant properties of bacterial ***ghost*** preparations enhance immune responses against envelope bound antigens, including T-cell activation and mucosal immunity. Since native and foreign antigens can be expressed in

the envelope complex of ***ghosts*** before E-mediated lysis, multiple antigens of various origins can be presented to the immune system simultaneously. The advantages of bacterial ***ghosts*** include the simplicity of the production method, safety, independence from the cold chain, and versatility as a combination vaccine.

IT Methods & Equipment
bacterial ***ghost*** system: drug delivery device

IT Miscellaneous Descriptors
mucosal immunity

L2 ANSWER 40 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2001:564814 CAPLUS <<LOGINID::20090617>>
DN 135:127159
TI Closure of bacterial ***ghosts*** by vesicle membrane fusion
IN ***Lubitz, Werner*** ; Paukner, Susanne
PA Austria
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001054672	A2	20010802	WO 2001-EP864	20010126
	WO 2001054672	A3	20020117		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 10003241	A1	20010802	DE 2000-10003241	20000126
	EP 1251835	A2	20021030	EP 2001-916954	20010126
	EP 1251835	B1	20080813		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CA 2423122	A1	20030319	CA 2001-2423122	20010126
	JP 2003521494	T	20030715	JP 2001-555650	20010126
	NZ 520655	A	20040924	NZ 2001-520655	20010126
	AU 2001244109	B2	20041202	AU 2001-244109	20010126
	AU 2001244109	B9	20050526		
	AT 404181	T	20080815	AT 2001-916954	20010126
	ES 2307602	T3	20081201	ES 2001-916954	20010126
	US 20030003511	A1	20030102	US 2002-181443	20020726
	US 6951756	B2	20051004		
PRAI	DE 2000-10003241	A	20000126		
	WO 2001-EP864	W	20010126		

AB The invention relates to a method for prodn. of closed bacterial ***ghosts*** , by means of vesicle membrane fusion and the corresponding bacterial ***ghosts*** . Active agents, for example, genetic material, cell components, pharmaceutical and agricultural agents and markers or dyes, may be packed in the closed bacterial ***ghosts*** . The metabolic functions and, optionally, reproductive viability of the bacterial ***ghosts*** can be re-established on packing genetic

material in the bacterial ***ghost*** . The closed ***ghosts*** can find application in the medical, agricultural and biotechnol. fields. Thus, Escherichia coli NM522 cells were transformed with plasmid pML1 and cultured; expression of lysis protein E was subsequently induced by raising the temp. from 28.degree. to 42.degree.. Centrifugation of the cells and resuspension in distd. water resulted in immediate lysis, producing ***ghosts*** . The ***ghost*** cells were washed lyophilized or frozen. Membrane vesicles were prepd. from harvested Escherichia coli NM522 cells; cells were disrupted in a French press, centrifuged; the supernatant was ultracentrifuged, the pellet that contained the vesicles was suspended in buffer. For loading the ***ghost*** cells, the active substance, e.g. ONPG, fluorescent-labeled DNA, was dissolved in the fusion buffer. Also vesicle membrane membranes were suspended in the fusion buffer; for the fusion with the bacterial host the mixt. was incubated at 37.degree.C in the presence of calcium ions overnight.

TI Closure of bacterial ***ghosts*** by vesicle membrane fusion

IN ***Lubitz, Werner*** ; Paukner, Susanne

AB The invention relates to a method for prodn. of closed bacterial ***ghosts*** , by means of vesicle membrane fusion and the corresponding bacterial ***ghosts*** . Active agents, for example, genetic material, cell components, pharmaceutical and agricultural agents and markers or dyes, may be packed in the closed bacterial ***ghosts*** . The metabolic functions and, optionally, reproductive viability of the bacterial ***ghosts*** can be re-established on packing genetic material in the bacterial ***ghost*** . The closed ***ghosts*** can find application in the medical, agricultural and biotechnol. fields. Thus, Escherichia coli NM522 cells were transformed with plasmid pML1. . . the temp. from 28.degree. to 42.degree.. Centrifugation of the cells and resuspension in distd. water resulted in immediate lysis, producing ***ghosts*** . The ***ghost*** cells were washed lyophilized or frozen. Membrane vesicles were prepd. from harvested Escherichia coli NM522 cells; cells were disrupted in. . . French press, centrifuged; the supernatant was ultracentrifuged, the pellet that contained the vesicles was suspended in buffer. For loading the ***ghost*** cells, the active substance, e.g. ONPG, fluorescent-labeled DNA, was dissolved in the fusion buffer. Also vesicle membrane membranes were suspended. . .

ST bacterium envelope ***ghost*** closure vesicle membrane fusion

IT Cell envelope
(bacterial, ***ghost*** ; closure of bacterial ***ghosts*** using)

IT Actinobacillus
Agrobacterium
Agrochemicals
Antitumor agents
Azotobacter
Biotechnology
Bordetella
Bradyrhizobium
Burkholderia
Cytolysis
Drug delivery systems
Drug targeting
Enterobacter
Erwinia
Escherichia coli
Fermentation

Francisella
Frankia
Fusion, biological
Gene therapy
Haemophilus
Helicobacter
Klebsiella
Liposomes
Membrane, biological
Pantoea
Pasteurella
Pseudomonas
Rhizobium
Rhizomonas
Salmonella
Serratia
Sphingomonas
Streptomyces
Vaccines
Vibrio
(closure of bacterial ***ghosts*** using)

IT Lipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(closure of bacterial ***ghosts*** using)

IT Peptides, biological studies
Polyoxyalkylenes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(closure of bacterial ***ghosts*** using)

IT 56-81-5, Glycerin, biological studies 67-68-5, Dimethylsulfoxide, biological studies 369-07-3, o-Nitrophenyl-.beta.-D-galactopyranoside 1461-15-0, Calcein 2321-07-5D, Fluorescein, DNA 5'-label 3520-42-1, Sulforhodamine B 7440-70-2, Calcium, biological studies 25322-68-3, Polyethyleneglycol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(closure of bacterial ***ghosts*** using)

L2 ANSWER 41 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:623585 CAPLUS <<LOGINID::20090617>>
DN 133:227782
TI Bacterial ***ghosts*** as carrier and targeting vehicles
IN Huter, Veronika; ***Lubitz, Werner***
PA Austria
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19909770	A1	20000907	DE 1999-19909770	19990305
CA 2370714	A1	20000914	CA 2000-2370714	20000303
WO 2000053163	A1	20000914	WO 2000-EP1906	20000303

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1158966	A1	20011205	EP 2000-912549	20000303
	EP 1158966	B1	20030611		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002538198	T	20021112	JP 2000-603652	20000303
	AT 242630	T	20030615	AT 2000-912549	20000303
	NZ 514408	A	20040130	NZ 2000-514408	20000303
	AU 778166	B2	20041118	AU 2000-34272	20000303
PRAI	DE 1999-19909770	A	19990305		
	WO 2000-EP1906	W	20000303		

AB Empty bacterial envelopes (***ghosts***), produced by controlled heterologous expression of a gene which effects a partial lysis of the cell membrane, are useful as carriers and targeting vehicles for active substances and markers. They may be administered via the natural infection pathways for pathogenic bacteria and are delivered specifically to the target tissues of the bacteria with high efficiency. Being empty, they can be loaded with active substances to a high degree. Agents which can be packaged in the ***ghosts*** include drugs, polypeptides, nucleic acids, agrochems., dyes, inks, and cosmetics; these may be immobilized by binding to specific receptors or binding sites incorporated into or anchored to the ***ghosts*** . Thus, Escherichia coli NM522 cells were transformed simultaneously with plasmid pML1 (contg. phage .phi.X174 gene E encoding a transmembrane protein which induces leakage of the cell contents) and plasmid pAV1 (contg. the 54 5'-terminal codons of gene E fused in-frame to a coding sequence for the protease factor Xa recognition sequence and to 160 codons of the streptavidin gene). Expression of the streptavidin gene was induced with 3 mM IPTG, and expression of lysis protein E was subsequently induced by raising the temp. from 28.degree. to 42.degree.. Centrifugation of the cells and resuspension in distd. water resulted in immediate lysis, producing ***ghosts*** to which streptavidin was anchored. These ***ghosts*** strongly bound biotinylated alk. phosphatase, FITC-biotin, and other biotinylated agents.

TI Bacterial ***ghosts*** as carrier and targeting vehicles

IN Huter, Veronika; ***Lubitz, Werner***

AB Empty bacterial envelopes (***ghosts***), produced by controlled heterologous expression of a gene which effects a partial lysis of the cell membrane, are useful as. . . Being empty, they can be loaded with active substances to a high degree. Agents which can be packaged in the ***ghosts*** include drugs, polypeptides, nucleic acids, agrochems., dyes, inks, and cosmetics; these may be immobilized by binding to specific receptors or binding sites incorporated into or anchored to the ***ghosts*** . Thus, Escherichia coli NM522 cells were transformed simultaneously with plasmid pML1 (contg. phage .phi.X174 gene E encoding a transmembrane protein. . . the temp. from 28.degree. to 42.degree.. Centrifugation of the cells and resuspension in distd. water resulted in immediate lysis, producing ***ghosts*** to which streptavidin was anchored. These ***ghosts*** strongly bound biotinylated alk. phosphatase, FITC-biotin, and other biotinylated agents.

ST bacteria ***ghost*** drug carrier targeting; streptavidin bacteria ***ghost*** drug carrier

IT Gene, microbial
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E, of phage .phi.X174, plasmid contg.; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active agent immobilization in matrix of; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Diagnosis
(agents; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Agrochemicals
Anti-infective agents
Antitumor agents
Autoimmune disease
Bacteria (Eubacteria)
Cell membrane
Cytolysis
Drug targeting
Dyes
Gene therapy
Genetic markers
Gram-negative bacteria
Gram-positive bacteria (Firmicutes)
Immobilization, biochemical
Vaccines
(bacterial ***ghosts*** as carrier and targeting vehicles)

IT Nucleic acids
Reporter gene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bacterial ***ghosts*** as carrier and targeting vehicles)

IT Avidins
Polysaccharides, biological studies
Receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bacterial ***ghosts*** as carrier and targeting vehicles)

IT Drug delivery systems
(carriers; bacterial ***ghosts*** as carrier and targeting vehicles)

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fluorescent-labeled; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Coliphage .phi.X174
(gene E protein of, lysis by; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy, polymers; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand-binding; bacterial ***ghosts*** as carrier and targeting vehicles)

IT Aggregation

(matrix formation by; bacterial ***ghosts*** as carrier and targeting vehicles)
IT Enzymes, uses
RL: CAT (Catalyst use); USES (Uses)
(matrix polymn. catalyzed by; bacterial ***ghosts*** as carrier and targeting vehicles)
IT Encapsulation
(microencapsulation; bacterial ***ghosts*** as carrier and targeting vehicles)
IT Plasmids
(streptavidin gene-contg.; bacterial ***ghosts*** as carrier and targeting vehicles)
IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(streptavidin-contg.; bacterial ***ghosts*** as carrier and targeting vehicles)
IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfates; bacterial ***ghosts*** as carrier and targeting vehicles)
IT 146397-20-8
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(DNA labeled with; bacterial ***ghosts*** as carrier and targeting vehicles)
IT 25988-63-0, Poly-L-lysine hydrobromide 35013-72-0, Biotin N-hydroxysuccinimide ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(bacterial ***ghosts*** as carrier and targeting vehicles)
IT 9004-54-0, Dextran, biological studies 9013-20-1, Streptavidin 25104-18-1, Poly-L-lysine 38000-06-5, Poly-L-lysine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bacterial ***ghosts*** as carrier and targeting vehicles)
IT 9001-78-9D, biotinylated 25104-18-1D, Poly-L-lysine, biotinylated 38000-06-5D, Poly-L-lysine, biotinylated 134759-22-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding of, to streptavidin-contg. bacterial ***ghosts*** ; bacterial ***ghosts*** as carrier and targeting vehicles)

L2 ANSWER 42 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 31
AN 2000:355995 BIOSIS <<LOGINID::20090617>>
DN PREV200000355995
TI Intramuscular immunization with genetically inactivated (***ghosts***) Actinobacillus pleuropneumoniae serotype 9 protects pigs against homologous aerosol challenge and prevents carrier state.
AU Hensel, Andreas [Reprint author]; Huter, Veronika; Katinger, Astrid; Raza, Peter; Strnistschie, Christine; Roesler, Uwe; Brand, Edith; ***Lubitz,*** Werner***
CS Veterinary Faculty, Institute of Animal Hygiene and Veterinary Public Health, University of Leipzig, D-04103, Leipzig, Germany
SO Vaccine, (1 July, 2000) Vol. 18, No. 26, pp. 2945-2955. print.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 16 Aug 2000

Last Updated on STN: 8 Jan 2002

AB Bacterial ***ghosts*** are empty cell envelopes achieved by the expression of a cloned bacteriophage lysis gene and, unlike classical bacterins, suffer no denaturing steps during their production. These properties may lead to a superior presentation of surface antigens to the immune system. Currently available porcine Actinobacillus pleuropneumoniae vaccines afford only minimal protection by decreasing mortality but not morbidity. Pigs which survive infection can still be carriers of the pathogen, so a herd once infected remains infected. Carrier pigs harbour A. pleuropneumoniae in their nasal cavities, in their tonsils, or within lung lesions. A dose-defined nose-only aerosol infection model for pigs was used to study the immunogenic and protective potential of systemic immunization with ***ghosts*** made from A. pleuropneumoniae serotype 9 reference strain CVI 13261 against an homologous aerogenous challenge. Pigs were vaccinated twice intramuscularly with a dose of 5 X 109 CFU ***ghosts*** (GVPs) or formalin-inactivated A. pleuropneumoniae bacterins (BVPs). After 2 weeks vaccinated pigs and non-vaccinated placebo controls (PCs) were challenged with a dose of 109 CFU by aerosol. The protective efficacy of immunization was evaluated by clinical, bacteriological, serological and post-mortem examinations. Bronchoalveolar lavage in pigs was performed during the experiment to obtain lavage samples (BALF) for assessment of local antibodies. Isotype-specific antibody responses in serum and BALF were determined by ELISAs based on whole-cell antigen. Immunization with ***ghosts*** did not cause clinical side-effects. After aerosol challenge PCs developed fever and pleuropneumonia. GVPs or BVPs were found to be fully protected against clinical disease or lung lesions in both vaccination groups, whereas colonization of the respiratory tract with A. pleuropneumoniae was only prevented in GVPs. Specific immunoglobins against A. pleuropneumoniae were not detectable in BALF after immunization. A significant systemic increase of IgM, IgA, IgG(Fc'), or IgG(H + L) antibodies reactive with A. pleuropneumoniae was measured in GVPs and BVPs when compared to the non-exposed controls. BVPs reached higher titers of IgG(Fc') and IgG(H + L) than GVPs. However, prevention of carrier state in GVPs coincided with a significant increase of serum IgA when compared to BVPs. These results suggest that immunization with ***ghosts*** , that bias antibody populations specific to non-denaturated surface antigens, may be more efficacious in protecting pigs against colonization and infection than bacterins.

TI Intramuscular immunization with genetically inactivated (***ghosts***) Actinobacillus pleuropneumoniae serotype 9 protects pigs against homologous aerosol challenge and prevents carrier state.

AU Hensel, Andreas [Reprint author]; Huter, Veronika; Katinger, Astrid; Raza, Peter; Strnistschie, Christine; Roesler, Uwe; Brand, Edith; ***Lubitz,*** ***Werner***

AB Bacterial ***ghosts*** are empty cell envelopes achieved by the expression of a cloned bacteriophage lysis gene and, unlike classical bacterins, suffer no. . . dose-defined nose-only aerosol infection model for pigs was used to study the immunogenic and protective potential of systemic immunization with ***ghosts*** made from A. pleuropneumoniae serotype 9 reference strain CVI 13261 against an homologous aerogenous challenge. Pigs were vaccinated twice intramuscularly with a dose of 5 X 109 CFU ***ghosts*** (GVPs) or formalin-inactivated A. pleuropneumoniae bacterins (BVPs). After 2 weeks vaccinated pigs and non-vaccinated placebo controls (PCs) were challenged with. . . of local antibodies. Isotype-specific antibody responses in serum and BALF were determined by ELISAs based on whole-cell antigen.

Immunization with ***ghosts*** did not cause clinical side-effects. After aerosol challenge PCs developed fever and pleuropneumonia. GVPs or BVPs were found to be. . . in GVPs coincided with a significant increase of serum IgA when compared to BVPs. These results suggest that immunization with ***ghosts*** , that bias antibody populations specific to non-denaturated surface antigens, may be more efficacious in protecting pigs against colonization and infection. . .

IT . . .
system, lavage; bronchiole: respiratory system, lavage; bronchus: respiratory system, lavage; serum: blood and lymphatics

IT Chemicals & Biochemicals
Actinobacillus pleuropneumoniae ***ghost*** : genetically inactivated, intramuscular immunization; Actinobacillus pleuropneumoniae vaccine: immunostimulant-drug; IgA [immunoglobulin A]; IgG [immunoglobulin G]; IgH [immunoglobulin H]; IgL [immunoglobulin L];. . .

L2 ANSWER 43 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 32

AN 2000:467776 BIOSIS <<LOGINID::20090617>>

DN PREV200000467776

TI Improved protection against lung colonization by Actinobacillus pleuropneumoniae ***ghosts*** : Characterization of a genetically inactivated vaccine.

AU Huter, Veronika; Hensel, Andreas; Brand, Edith; ***Lubitz, Werner*** [Reprint author]

CS Section for Microbiology and Biotechnology, Biocenter, Institute of Microbiology and Genetics, University of Vienna, A-1030, Vienna, Austria

SO Journal of Biotechnology, (29 September, 2000) Vol. 83, No. 1-2, pp. 161-172. print.
CODEN: JBITD4. ISSN: 0168-1656.

DT Article

LA English

ED Entered STN: 1 Nov 2000
Last Updated on STN: 10 Jan 2002

AB Pigs immunized with Actinobacillus pleuropneumoniae ***ghosts*** or a formalin-inactivated bacterin were found to be protected against clinical disease in both vaccination groups, whereas colonization of the lungs with A. pleuropneumoniae was only prevented in ***ghost*** -vaccinated pigs. Bacterial ***ghosts*** are empty cell envelopes created by the expression of a cloned bacteriophage lysis gene and, unlike formalin-inactivated bacteria, suffer no denaturing steps during their production. This quality may lead to a superior presentation of surface antigens to the immune system. Analysis by SDS-PAGE and immunoblotting of the two vaccine preparations revealed different contents of antigenic proteins. In order to better understand the immunogenic properties of A. pleuropneumoniae ***ghosts*** and formalin-inactivated bacteria, we compared the serum antibody response induced in both treatment groups. Immune sera were tested on whole cell antigen or purified virulence factors including outer membrane protein preparations (OMPs), outer membrane lipoprotein OmlA1, transferrin binding proteins (TfbA1, TfbA7 and TfbB) and Apx toxins (ApxI, II and III). SDS-PAGE and immunoblots revealed no specific antibody response against the single virulence factors tested in any vaccinated animal. The two vaccination groups showed different recognition patterns of whole cell antigen and OMP-enriched preparations. A 100 kDa protein was recognized significantly stronger by ***ghost*** -vaccinated pigs than convalescent pigs. This

unique antibody population induced by ***ghosts*** could play a determining role in the prevention of lung colonization. The same 100 kDa antigen was recognized by ***ghost*** -sera in homologous as well as heterologous serotype A. pleuropneumoniae protein preparations. Indications for a crossprotective potential in the ***ghost*** vaccine were supported by studies on rabbit hyperimmune sera.

TI Improved protection against lung colonization by Actinobacillus pleuropneumoniae ***ghosts*** : Characterization of a genetically inactivated vaccine.

AU Huter, Veronika; Hensel, Andreas; Brand, Edith; ***Lubitz, Werner*** [Reprint author]

AB Pigs immunized with Actinobacillus pleuropneumoniae ***ghosts*** or a formalin-inactivated bacterin were found to be protected against clinical disease in both vaccination groups, whereas colonization of the lungs with A. pleuropneumoniae was only prevented in ***ghost*** -vaccinated pigs. Bacterial ***ghosts*** are empty cell envelopes created by the expression of a cloned bacteriophage lysis gene and, unlike formalin-inactivated bacteria, suffer no. . . two vaccine preparations revealed different contents of antigenic proteins. In order to better understand the immunogenic properties of A. pleuropneumoniae ***ghosts*** and formalin-inactivated bacteria, we compared the serum antibody response induced in both treatment groups. Immune sera were tested on whole. . . showed different recognition patterns of whole cell antigen and OMP-enriched preparations. A 100 kDa protein was recognized significantly stronger by ***ghost*** -vaccinated pigs than convalescent pigs. This unique antibody population induced by ***ghosts*** could play a determining role in the prevention of lung colonization. The same 100 kDa antigen was recognized by ***ghost*** -sera in homologous as well as heterologous serotype A. pleuropneumoniae protein preparations. Indications for a crossprotective potential in the ***ghost*** vaccine were supported by studies on rabbit hyperimmune sera.

IT . . .
Coordination and Homeostasis); Infection; Veterinary Medicine (Medical Sciences); Pharmacology; Respiratory System (Respiration)

IT Parts, Structures, & Systems of Organisms
bacterial ***ghosts*** , uses; lungs: respiratory system, bacterial colonization, protection

IT Chemicals & Biochemicals
antigens; bacterial proteins; bacterial vaccines: development, preparation; genetically inactivated. . .

L2 ANSWER 44 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 33

AN 2000:42619 BIOSIS <<LOGINID::20090617>>

DN PREV200000042619

TI Bacterial cell envelopes (***ghosts***) but not S-layers activate human endothelial cells (HUVECs) through sCD14 and LBP mechanism.

AU Furst-Ladani, Shayesteh [Reprint author]; Redl, Heinz; Haslberger, Alexander; ***Lubitz, Werner*** ; Messner, Paul; Sleytr, Uwe B.; Schlag, Gunther

CS Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Donaueschingenstrasse 13, 1200, Vienna, Austria

SO Vaccine, (Oct., 1999) Vol. 18, No. 5-6, pp. 440-448. print.
CODEN: VACCDE. ISSN: 0264-410X.

DT Article

LA English

ED Entered STN: 26 Jan 2000
Last Updated on STN: 31 Dec 2001

AB Bacterial cell-envelopes (called ***ghosts***) and surface layers (S-layers) are discussed to be used as vaccines and/or adjuvants, consequently it is necessary to find out which immunomodulatory mediators are induced in human cells. The present work focuses on the effects of ***ghosts*** (Escherichia coli O26:B6), S-layers (Bacillus stearothermophilus) in comparison with LPS and antibiotic-inactivated whole bacteria (E. coli O26:B6) on human umbilical vein endothelial cells (HUVEC) with regard to the release of interleukin 6 (IL-6) and the expression of surface E-selectin and the role of lipopolysaccharide binding protein (LBP), soluble CD14 (sCD14) and serum for this activation. Endothelial cells responded to ***ghosts*** , whole bacteria and LPS with IL-6 release up to 15000 pg/ml and surface E-selectin expression, while in contrast the response to S-layers with IL-6 release up to 500 pg/ml was very weak. Compared to LPS, 10-100-fold higher concentrations of bacterial ***ghosts*** and whole bacteria were required to induce the cytokine synthesis and E-selectin expression. IL-6 release and E-selectin expression of HUVECs were reduced in the absence of serum and equivalent to unstimulated samples. We have also studied the role of CD14 and LBP for the activation of endothelial cells using antiCD14 and antiLBP antibodies (Ab). AntiCD14 and antiLBP Ab both inhibited IL-6 release and E-selectin expression in a dose dependent manner after stimulation with ***ghosts*** , whole bacteria and LPS but had no effect on S-layers stimulated cells. AntiCD14 Ab inhibited more effectively than antiLBP Ab. These findings suggest that bacterial ***ghosts*** but not S-layers activate HUVECs through sCD14 and LBP dependent mechanisms.

TI Bacterial cell envelopes (***ghosts***) but not S-layers activate human endothelial cells (HUVECs) through sCD14 and LBP mechanism.

AU Furst-Ladani, Shayesteh [Reprint author]; Redl, Heinz; Haslberger, Alexander; ***Lubitz, Werner*** ; Messner, Paul; Sleytr, Uwe B.; Schlag, Gunther

AB Bacterial cell-envelopes (called ***ghosts***) and surface layers (S-layers) are discussed to be used as vaccines and/or adjuvants, consequently it is necessary to find out which immunomodulatory mediators are induced in human cells. The present work focuses on the effects of ***ghosts*** (Escherichia coli O26:B6), S-layers (Bacillus stearothermophilus) in comparison with LPS and antibiotic-inactivated whole bacteria (E. coli O26:B6) on human umbilical. . . and the role of lipopolysaccharide binding protein (LBP), soluble CD14 (sCD14) and serum for this activation. Endothelial cells responded to ***ghosts*** , whole bacteria and LPS with IL-6 release up to 15000 pg/ml and surface E-selectin expression, while in contrast the response. . . to S-layers with IL-6 release up to 500 pg/ml was very weak. Compared to LPS, 10-100-fold higher concentrations of bacterial ***ghosts*** and whole bacteria were required to induce the cytokine synthesis and E-selectin expression. IL-6 release and E-selectin expression of HUVECs. . . (Ab). AntiCD14 and antiLBP Ab both inhibited IL-6 release and E-selectin expression in a dose dependent manner after stimulation with ***ghosts*** , whole bacteria and LPS but had no effect on S-layers stimulated cells. AntiCD14 Ab inhibited more effectively than antiLBP Ab. These findings suggest that bacterial ***ghosts*** but not S-layers activate HUVECs through sCD14 and LBP dependent mechanisms.

IT . . .
System (Chemical Coordination and Homeostasis)

IT Chemicals & Biochemicals
CD14 antigen: soluble; E-selectin protein: expression; IL-6

[interleukin-6]: synthesis; bacterial cell-envelope [***ghost***]: immunostimulant-drug, pharmaceutical adjunct-drug, vaccine; bacterial surface layer [bacterial S-layer]: immunostimulant-drug, pharmaceutical adjunct-drug, vaccine; lipopolysaccharide binding protein [LPB binding protein]

L2 ANSWER 45 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 34
AN 1999:216945 BIOSIS <<LOGINID::20090617>>
DN PREV199900216945
TI Altered temperature induction sensitivity of the lambda pR/cI857 system for controlled gene E expression in Escherichia coli.
AU Jechlinger, Wolfgang [Reprint author]; Szostak, Michael P.; Witte, Angela; ***Lubitz, Werner***
CS EVAX Technologies, Fraunhoferstr. 10, D-82152, Munich, Germany
SO FEMS Microbiology Letters, (April 15, 1999) Vol. 173, No. 2, pp. 347-352. print.
CODEN: FMLED7. ISSN: 0378-1097.
DT Article
LA English
ED Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999
AB Cell lysis of Gram-negative bacteria can be efficiently achieved by expression of the cloned lysis gene E of bacteriophage PhiX174. Gene E expression is tightly controlled by the rightward lambdapR promoter and the temperature-sensitive repressor cI857 on lysis plasmid pAW12. The resulting empty bacterial cell envelopes, called bacterial ***ghosts*** , are currently under investigation as candidate vaccines. Expression of gene E is stringently repressed at temperatures up to 30degreeC, whereas gene E expression, and thus cell lysis, is induced at temperatures higher than 30degreeC due to thermal inactivation of the cI857 repressor. As a consequence, the production of ***ghosts*** requires that bacteria have to be grown at 28degreeC before the lysis process is induced. In order to reflect the growth temperature of pathogenic bacteria in vivo, it seemed favorable to extend the heat stability of the lambda pR promoter/cI857 repressor system, allowing pathogens to grow at 37degreeC before induction of lysis. In this study we describe a mutation in the lambda pR promoter, which allows stringent repression of gene E expression at temperatures up to 36degreeC, but still permits induction of cell lysis at 42degreeC.
AU Jechlinger, Wolfgang [Reprint author]; Szostak, Michael P.; Witte, Angela; ***Lubitz, Werner***
AB. . . rightward lambdapR promoter and the temperature-sensitive repressor cI857 on lysis plasmid pAW12. The resulting empty bacterial cell envelopes, called bacterial ***ghosts*** , are currently under investigation as candidate vaccines. Expression of gene E is stringently repressed at temperatures up to 30degreeC, whereas. . . induced at temperatures higher than 30degreeC due to thermal inactivation of the cI857 repressor. As a consequence, the production of ***ghosts*** requires that bacteria have to be grown at 28degreeC before the lysis process is induced. In order to reflect the. . .
IT Miscellaneous Descriptors
bacterial cell envelopes: candidate vaccine; bacterial ***ghosts*** : candidate vaccine; cell lysis; gene expression; lambda p-R/cI857 repressor system: heat stability, temperature induction sensitivity; safety cassette; temperature; vaccine development

L2 ANSWER 46 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 35

AN 1999:468971 BIOSIS <<LOGINID::20090617>>

DN PREV199900468971

TI Pigs aerogenously immunized with genetically inactivated (***ghosts***) or irradiated Actinobacillus pleuropneumoniae are protected against a homologous aerosol challenge despite differing in pulmonary cellular and antibody responses.

AU Katinger, Astrid; ***Lubitz, Werner*** ; Szostak, Michael P.; Stadler, Maria; Klein, Reinhard; Indra, Alexander; Huter, Veronika; Hensel, Andreas [Reprint author]

CS Institute of Animal Hygiene and Veterinary Public Health, University of Leipzig, Semmelweisstr. 4, D-04103, Leipzig, Germany

SO Journal of Biotechnology, (Aug. 20, 1999) Vol. 73, No. 2-3, pp. 251-260. print.
CODEN: JBITD4. ISSN: 0168-1656.

DT Article

LA English

ED Entered STN: 9 Nov 1999
Last Updated on STN: 9 Nov 1999

AB Aerosol immunization is a safe way to induce complete protection against pleuropneumonia in pigs caused by the lung pathogenic bacterium Actinobacillus pleuropneumoniae. In order to determine the local immune responses of vaccines in concomitant with protection, lung lining fluid before and 3 weeks after immunization from pigs immunized three times with aerosols of either genetically inactivated ***ghosts*** which represent whole cell envelope preparations, or irradiated bacteria were examined following an homologous aerosol challenge. Specific antibody isotypes in the bronchoalveolar lavage were assayed by whole cell ELISAs. Total and relative numbers of cells including lymphocyte subsets were determined. In both vaccinated groups a net influx of plasma cells and lymphocytes, as well as a significant increase of specific IgG occurred. Concurrently, the CD4+/CD8+ ratio was found to increase after aerosol immunization. The lymphocyte subsets of IgG+ and IgA+ cells were found significantly higher in the group immunized with irradiated bacteria when compared to pigs immunized with bacterial ***ghosts*** . The latter group showed a significant increase of IgA, IgM, and a net influx of lymphoid blasts and granulocytes in the bronchoalveolar lining fluid. Although differences between the local immune responses of both immunized groups occurred, a significant increase of specific IgG and a net influx of plasma cells and lymphocytes were found to be associated with complete protection against a homologous aerosol challenge infection.

TI Pigs aerogenously immunized with genetically inactivated (***ghosts***) or irradiated Actinobacillus pleuropneumoniae are protected against a homologous aerosol challenge despite differing in pulmonary cellular and antibody responses.

AU Katinger, Astrid; ***Lubitz, Werner*** ; Szostak, Michael P.; Stadler, Maria; Klein, Reinhard; Indra, Alexander; Huter, Veronika; Hensel, Andreas [Reprint author]

AB. . . lung lining fluid before and 3 weeks after immunization from pigs immunized three times with aerosols of either genetically inactivated ***ghosts*** which represent whole cell envelope preparations, or irradiated bacteria were examined following an homologous aerosol challenge. Specific antibody isotypes in. . . IgA+ cells were found significantly higher in the group immunized with irradiated bacteria when compared to pigs immunized with bacterial ***ghosts*** . The latter group showed a significant increase of IgA, IgM, and a net influx of

lymphoid blasts and granulocytes in. . .
IT Methods & Equipment
aerosol immunization: immunization method, vaccine delivery method; genetically inactivated ***ghost*** aerosol immunization: immunization method
IT Miscellaneous Descriptors
antibody response; immune response; vaccine development

L2 ANSWER 47 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 36
AN 2000:9740 BIOSIS <<LOGINID::20090617>>
DN PREV200000009740
TI Bacterial ***ghosts*** as drug carrier and targeting vehicles.
AU Huter, Veronika [Reprint author]; Szostak, Michael P.; Gampfer, Joerg; Prethaler, Saskia; Wanner, Gerhard; Gabor, Franz; ***Lubitz, Werner***
CS Institute of Microbiology and Genetics, University of Vienna, Dr. Bohrgasse 9, A-1030, Vienna, Austria
SO Journal of Controlled Release, (Aug. 27, 1999) Vol. 61, No. 1-2, pp. 51-63. print.
CODEN: JCREEC. ISSN: 0168-3659.
DT Article
LA English
ED Entered STN: 23 Dec 1999
Last Updated on STN: 31 Dec 2001
AB A novel system for the packaging of drugs as well as vaccines is presented. Bacterial ***ghosts*** are intact, non-denatured bacterial envelopes that are created by lysis of bacteria through the expression of cloned phage PhiX174 gene E. Inhibition of induced E-mediated lysis by MgSO4, harvesting of cells by centrifugation, and resuspension in low-ionic-strength buffers leads to rapid, violent lysis and results in empty bacterial envelopes with large (approximately 1 mum in diameter) openings. The construction of plasmid pAV1, which encodes a streptavidin fusion protein with an N-terminal membrane anchor sequence, allows the loading of the inner side of the cytoplasmic membrane with streptavidin. The functionality and efficacy of binding of even large biotinylated compounds in such streptavidin ***ghosts*** (SA- ***ghosts***) was assessed using the enzyme alkaline phosphatase. The successful binding of biotinylated fluorescent dextran, as well as fluorescent DNA complexed with biotinylated polylysine, w as demonstrated microscopically. The display by bacterial ***ghosts*** of morphological and antigenic surface structures of their living counterparts permits their attachment to target tissues such as the mucosal surfaces of the gastrointestinal and respiratory tract, and their uptake by phagocytes and M cells. In consequence, SA- ***ghosts*** are proposed as drug carriers for site-specific drug delivery.
TI Bacterial ***ghosts*** as drug carrier and targeting vehicles.
AU Huter, Veronika [Reprint author]; Szostak, Michael P.; Gampfer, Joerg; Prethaler, Saskia; Wanner, Gerhard; Gabor, Franz; ***Lubitz, Werner***
AB A novel system for the packaging of drugs as well as vaccines is presented. Bacterial ***ghosts*** are intact, non-denatured bacterial envelopes that are created by lysis of bacteria through the expression of cloned phage PhiX174 gene. . . of the cytoplasmic membrane with streptavidin. The functionality and efficacy of binding of even large biotinylated compounds in such streptavidin ***ghosts*** (SA- ***ghosts***) was assessed using the enzyme alkaline phosphatase. The successful binding of biotinylated fluorescent dextran, as well as fluorescent DNA complexed with biotinylated polylysine, w as demonstrated

microscopically. The display by bacterial ***ghosts*** of morphological and antigenic surface structures of their living counterparts permits their attachment to target tissues such as the mucosal surfaces of the gastrointestinal and respiratory tract, and their uptake by phagocytes and M cells. In consequence, SA- ***ghosts*** are proposed as drug carriers for site-specific drug delivery.
IT Miscellaneous Descriptors
streptavidin- ***ghost*** : drug carrier, drug targeting vehicle

L2 ANSWER 48 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 37
AN 1997:180858 BIOSIS <<LOGINID::20090617>>
DN PREV199799472571
TI Endotoxicity does not limit the use of bacterial ***ghosts*** as candidate vaccines.
AU Mader, Horst J.; Szostak, Michael P.; Hensel, Andreas; ***Lubitz,*** *** Werner*** ; Haslberger, Alexander G. [Reprint author]
CS Inst. Microbiol. Genetics, Univ. Vienna, Biocenter Dr. Bohrgasse 9, Vienna, A-1030, Austria
SO Vaccine, (1997) Vol. 15, No. 2, pp. 195-202.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 24 Apr 1997
Last Updated on STN: 24 Apr 1997
AB Gram-negative bacterial ***ghosts*** produced by controlled expression of the plasmid-encoded lysis gene E offers a promising approach in non-living vaccine technology. Bacterial cell wall complex and hence the antigenic determinants of the living cells are not affected by denaturation due to cell killing. However, the endotoxin content of the Gram-negative cell wall has been discussed as a potential problem for this kind of whole cell or envelope vaccines. Here we show that bacterial ***ghosts*** prepared from Escherichia coli O26:B6 and Salmonella typhimurium C5 induce dose-dependent antibody responses against bacterial cells or their corresponding lipopolysaccharides (LPS) in doses 25 ng kg-1 when administered intravenously to rabbits in a standard immunization protocol. No differences between the immune responses of the rabbits were observed when comparing equivalent doses of bacterial ***ghosts*** and antibiotic-treated whole cells. The results indicate that the bacterial ***ghosts*** exhibit all the antigenic properties of the living cells. No significant fever responses in rabbits have been recorded in doses of lt 250 ng kg-1 E. coli O26:B6 ***ghosts*** and up to doses of 250 ng kg-1 S. typhimurium C5 ***ghosts*** when applying test methods recommended by the US pharmacopoeia. These findings correlate with cell culture experiments where doses 100 ng ml-1 of bacterial ***ghosts*** were needed for the release of tumour necrosis factor alpha (TNF-alpha) and prostaglandin E-2 (PGE-2) from RAW mouse macrophage cultures. Free LPS of Salmonella abortus equi commonly used as a LPS-standard, however, stimulated TNF-alpha and PGE-2 synthesis of RAW cells in doses of 1 ng ml-1. The endotoxic activity of our bacterial preparations analysed by a standard limulus amoebocyte lysate and 2-keto-3-deoxyoctonate assay correlated with the capacity to stimulate the release of PGE-2 and TNF-alpha in RAW mouse macrophage cultures and the endotoxic responses in rabbits. It can be concluded that these in vitro systems can be used as easy predictive test systems for preparations of bacterial vaccines, particularly for bacterial ***ghosts*** .
TI Endotoxicity does not limit the use of bacterial ***ghosts*** as

candidate vaccines.
AU Mader, Horst J.; Szostak, Michael P.; Hensel, Andreas; ***Lubitz,*** ***Werner*** ; Haslberger, Alexander G. [Reprint author]
AB Gram-negative bacterial ***ghosts*** produced by controlled expression of the plasmid-encoded lysis gene E offers a promising approach in non-living vaccine technology. Bacterial cell. . . been discussed as a potential problem for this kind of whole cell or envelope vaccines. Here we show that bacterial ***ghosts*** prepared from Escherichia coli O26:B6 and Salmonella typhimurium C5 induce dose-dependent antibody responses against bacterial cells or their corresponding lipopolysaccharides. . . standard immunization protocol. No differences between the immune responses of the rabbits were observed when comparing equivalent doses of bacterial ***ghosts*** and antibiotic-treated whole cells. The results indicate that the bacterial ***ghosts*** exhibit all the antigenic properties of the living cells. No significant fever responses in rabbits have been recorded in doses of lt 250 ng kg-1 E. coli O26:B6 ***ghosts*** and up to doses of 250 ng kg-1 S. typhimurium C5 ***ghosts*** when applying test methods recommended by the US pharmacopoeia. These findings correlate with cell culture experiments where doses 100 ng ml-1 of bacterial ***ghosts*** were needed for the release of tumour necrosis factor alpha (TNF-alpha) and prostaglandin E-2 (PGE-2) from RAW mouse macrophage cultures.. . . these in vitro systems can be used as easy predictive test systems for preparations of bacterial vaccines, particularly for bacterial ***ghosts*** .
IT Miscellaneous Descriptors
ANTIGENICITY; BACTERIAL ***GHOSTS*** ; C5; DOSE-DEPENDENT ANTIBODY RESPONSE; ENDOTOXICITY; ENDOTOXIN; IMMUNE SYSTEM; LIPOPOLYSACCHARIDES; MACROPHAGE; O26:B6; PROSTAGLANDIN E-2; RELEASE; TNF-ALPHA; TOXICOLOGY; TUMOR NECROSIS FACTOR-ALPHA

L2 ANSWER 49 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 38
AN 1996:123868 BIOSIS <<LOGINID::20090617>>
DN PREV199698696003
TI Bacterial ***ghosts*** : Non-living candidate vaccines.
AU Szostak, Michael P.; Hensel, Andreas; Eko, Francis O.; Klein, Reinhard; Auer, Tatjana; Mader, Horst; Haslberger, Alexander; Bunka, Sebastian; Wanner, Gerhard; ***Lubitz, Werner*** [Reprint author]
CS Inst. Microbiol. Genetics, Univ. Vienna, Dr. Bohrgasse 9, A-1030 Vienna, Austria
SO Journal of Biotechnology, (1996) Vol. 44, No. 1-3, pp. 161-170. CODEN: JBITD4. ISSN: 0168-1656.
DT Article
LA English
ED Entered STN: 27 Mar 1996
Last Updated on STN: 27 Mar 1996
AB Expression of cloned PhiX174 gene E in bacteria results in lysis of bacteria. It is unique among phage lysis systems as it introduces a transmembrane tunnel structure through the cell envelope complex of Gram-negative bacteria. The resulting bacterial ***ghosts*** have intact envelope structures devoid of cytoplasmic contents. E-mediated lysis has been achieved in a variety of Gram-negative bacteria including Escherichia coli, Salmonella typhimurium, Vibrio cholerae, Klebsiella pneumoniae, and Actinobacillus pleuropneumoniae. Such ***ghosts*** , derived from human or animal pathogens, have been proposed as non-living candidate vaccines and represent an alternative to heat or chemically

inactivated bacteria. In 'recombinant ***ghosts*** ', foreign proteins (e.g., vital proteins) are inserted into the inner membrane via specific N-, or C-, or N- and C-terminal anchor sequences prior to lysis. Relevant advantages of (recombinant) bacterial ***ghosts*** as immunogens include: (i) inactivation procedures that denature relevant immunogenic determinants are not employed in the production of ***ghosts*** used as vaccines or as carriers of relevant antigens; (ii) the recombinant proteins are inserted into a highly immune stimulatory environment; (iii) there is no size limitation of the foreign protein moieties: multiple antigenic determinants can be presented simultaneously; (iv) bacterial ***ghosts*** can be produced inexpensively in large quantities; (v) (recombinant) ***ghosts*** are stable for long periods of time and do not require the cold chain storage system. Intraperitoneal, subcutaneous or intramuscular applications of recombinant ***ghosts*** in experimental animals induced specific humoral and cellular immune responses against bacterial and viral components. Initial aerosol vaccinations of swine with ***ghosts*** from Actinobacillus pleuropneumoniae showed that protective immunity can be established by this route of application and that the well-preserved surface structures of ***ghosts*** obtained by E-mediated lysis are able to target the mucosal immune system.

TI Bacterial ***ghosts*** : Non-living candidate vaccines.

AU. . . Szostak, Michael P.; Hensel, Andreas; Eko, Francis O.; Klein, Reinhard; Auer, Tatjana; Mader, Horst; Haslberger, Alexander; Bunka, Sebastian; Wanner, Gerhard; ***Lubitz, Werner*** [Reprint author]

AB. . . lysis systems as it introduces a transmembrane tunnel structure through the cell envelope complex of Gram-negative bacteria. The resulting bacterial ***ghosts*** have intact envelope structures devoid of cytoplasmic contents. E-mediated lysis has been achieved in a variety of Gram-negative bacteria including Escherichia coli, Salmonella typhimurium, Vibrio cholerae, Klebsiella pneumoniae, and Actinobacillus pleuropneumoniae. Such ***ghosts*** , derived from human or animal pathogens, have been proposed as non-living candidate vaccines and represent an alternative to heat or chemically inactivated bacteria. In 'recombinant ***ghosts*** ', foreign proteins (e.g., vital proteins) are inserted into the inner membrane via specific N-, or C-, or N- and C-terminal anchor sequences prior to lysis. Relevant advantages of (recombinant) bacterial ***ghosts*** as immunogens include: (i) inactivation procedures that denature relevant immunogenic determinants are not employed in the production of ***ghosts*** used as vaccines or as carriers of relevant antigens; (ii) the recombinant proteins are inserted into a highly immune stimulatory. . . (iii) there is no size limitation of the foreign protein moieties: multiple antigenic determinants can be presented simultaneously; (iv) bacterial ***ghosts*** can be produced inexpensively in large quantities; (v) (recombinant) ***ghosts*** are stable for long periods of time and do not require the cold chain storage system. Intraperitoneal, subcutaneous or intramuscular applications of recombinant ***ghosts*** in experimental animals induced specific humoral and cellular immune responses against bacterial and viral components. Initial aerosol vaccinations of swine with ***ghosts*** from Actinobacillus pleuropneumoniae showed that protective immunity can be established by this route of application and that the well-preserved surface structures of ***ghosts*** obtained by E-mediated lysis are able to target the mucosal immune system.

L2 ANSWER 50 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN DUPLICATE 39
AN 1994:546238 BIOSIS <<LOGINID::20090617>>
DN PREV199598005786
TI Immunogenicity of Vibrio cholerae ***ghosts*** following intraperitoneal immunization of mice.
AU Eko, Francis O. [Reprint author]; Hensel, Andreas; Bunka, Sebastian; ***Lubitz, Werner***
CS Inst. Microbiol. Genet., Univ. Vienna, Biocent., Dr. Bohrgasse 9, A-1030 Vienna, Austria
SO Vaccine, (1994) Vol. 12, No. 14, pp. 1330-1334.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 22 Dec 1994
Last Updated on STN: 22 Dec 1994
AB The immunogenic potential of Vibrio cholerae ***ghosts*** (VCG) in comparison with heat-killed whole-cell vibrios (WCV) was evaluated after intraperitoneal immunization of adult mice. Swiss white mice received four doses of VCG or VCG or WCV intraperitoneally, consisting of 500 mu-g of lyophilized material in 200 mu-l of phosphate-buffered saline (PBS), pH 7.4. The control group received 200 mu-l of PBS. Serum samples were collected from all mice on the day of immunization and on days 14, 24, 35 and 62 postimmunization. Sera were examined for vibriocidal antibodies by the microtitre and tube-dilution methods and Vibrio-specific serum IgG antibodies were assessed by ELISA. IgG antibodies to intact WCV were detected in sera from all animals immunized with VCG or WCV. The response was specific and of high magnitude. Significantly higher antibody responses were obtained when sera from both VCG- and WCV-immunized mice were titrated against VCG. The immunogenicity of VCG in evoking serum IgG responses was higher than that of WCV. However, the immunogenicity of the two antigen preparations was comparable in terms of seroconversion for vibriocidal antibodies. These results demonstrate that VCG administered intraperitoneally evoke Vibrio-specific serum IgG responses as well as vibriocidal antibody activity in mice.
TI Immunogenicity of Vibrio cholerae ***ghosts*** following intraperitoneal immunization of mice.
AU Eko, Francis O. [Reprint author]; Hensel, Andreas; Bunka, Sebastian; ***Lubitz, Werner***
AB The immunogenic potential of Vibrio cholerae ***ghosts*** (VCG) in comparison with heat-killed whole-cell vibrios (WCV) was evaluated after intraperitoneal immunization of adult mice. Swiss white mice received. . .

L2 ANSWER 51 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 40
AN 1994:537037 BIOSIS <<LOGINID::20090617>>
DN PREV199497550037
TI Production of Vibrio cholerae ***ghosts*** (VCG) by expression of a cloned phage lysis gene: Potential for vaccine development.
AU Eko, Francis O. [Reprint author]; Szostak, Michael P.; Wanner, Gerhard; ***Lubitz, Werner***
CS Inst. Microbiol. Genet., Univ. Vienna, Biocenter, Dr Bohrgasse 9, 1030 Vienna, Austria
SO Vaccine, (1994) Vol. 12, No. 13, pp. 1231-1237.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English

ED Entered STN: 15 Dec 1994
Last Updated on STN: 15 Dec 1994
AB The protein E-specific lysis mechanism of the Escherichia coli-specific bacteriophage PhiX174 was employed to produce Vibrio cholerae ***ghosts*** (VCG). VCG consist of both rounded and collapsed cells that have lost their cytoplasmic contents through an E-specific hole in the cell envelope. These ***ghosts*** are proposed as nonliving material for immunization against cholera. A specific membrane anchor sequence was used to insert the human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT) fusion protein into the cell envelope of V. cholerae. The identity of the expression products was confirmed by Western blot analysis employing an RT-specific monoclonal antibody). HIV-1 RT was chosen as a model for the purpose of evaluating heterologous gene expression in V. cholerae and the carrier potential of VCG. Intraperitoneal immunization of mice was used to evaluate the immunogenic potential of VCG. Preliminary results showed significant seroconversions to intact whole-cell vibrio antigens in mice immunized with VCG or a heat-killed whole-cell vibrio preparation.
TI Production of Vibrio cholerae ***ghosts*** (VCG) by expression of a cloned phage lysis gene: Potential for vaccine development.
AU Eko, Francis O. [Reprint author]; Szostak, Michael P.; Wanner, Gerhard; ***Lubitz, Werner***
AB The protein E-specific lysis mechanism of the Escherichia coli-specific bacteriophage PhiX174 was employed to produce Vibrio cholerae ***ghosts*** (VCG). VCG consist of both rounded and collapsed cells that have lost their cytoplasmic contents through an E-specific hole in the cell envelope. These ***ghosts*** are proposed as nonliving material for immunization against cholera. A specific membrane anchor sequence was used to insert the human. . .

L2 ANSWER 52 OF 54 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 41
AN 1993:469451 BIOSIS <<LOGINID::20090617>>
DN PREV199345092576
TI Immune response against recombinant bacterial ***ghosts*** carrying HIV-1 reverse transcriptase.
AU Szostak, Michael P.; Auer, Tatiana; ***Lubitz, Werner***
CS Inst. Microbiol. Genetics, Univ. Vienan, A-1030 Vienna, Austria
SO Ginsberg, H. S. [Editor]; Brown, F. [Editor]; Chanok, R. M. [Editor]; Lerner, R. A. [Editor]. Vaccines (Cold Spring Harbor), (1993) pp. 419-425. Vaccines (Cold Spring Harbor); Modern approaches to new vaccines including prevention of AIDS.
Publisher: Cold Spring Harbor Laboratory Press, 10 Skyline Drive, Plainview, New York 11803, USA. Series: Vaccines (Cold Spring Harbor). Meeting Info.: Tenth Annual Meeting. Cold Spring Harbor, New York, USA. September 1992.
ISSN: 0899-4056. ISBN: 0-87969-383-5.
DT Article
Conference; (Meeting)
LA English
ED Entered STN: 11 Oct 1993
Last Updated on STN: 11 Oct 1993
TI Immune response against recombinant bacterial ***ghosts*** carrying HIV-1 reverse transcriptase.
AU Szostak, Michael P.; Auer, Tatiana; ***Lubitz, Werner***

L2 ANSWER 53 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1992:1761 CAPLUS <<LOGINID::20090617>>
DN 116:1761
OREF 116:363a,366a
TI Membrane-anchoring of heterologous proteins in recombinant hosts for use as antigens
IN ***Lubitz, Werner*** ; Szostak, Michael P.
PA Boehringer Mannheim G.m.b.H., Germany
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9113155	A1	19910905	WO 1991-EP308	19910219
	W: AU, FI, HU, JP, SU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	DE 4005874	A1	19911107	DE 1990-4005874	19900224
	AU 9172373	A	19910918	AU 1991-72373	19910219
	EP 516655	A1	19921209	EP 1991-903789	19910219
	EP 516655	B1	19940504		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05503014	T	19930527	JP 1991-503980	19910219
	JP 3238396	B2	20011210		
	AT 105335	T	19940515	AT 1991-903789	19910219
	US 5470573	A	19951128	US 1992-924028	19920930
PRAI	DE 1990-4005874	A	19900224		
	EP 1991-903789	A	19910219		
	WO 1991-EP308	A	19910219		

AB Antigenic proteins are prepd. with a Gram-neg. bacteria contg. a gene encoding a lytic protein by expression of a chimeric gene for a fusion protein of a membrane-anchoring domain and the antigen. Plasmid pAV5 encoding a streptavidin-phage MS2 protein L fusion protein and a plasmid contg. the protein E gene of phage .phi.X174 under control of the temp. sensitive .lambda. repressor-.lambda. promoter/operator system were prepd. Escherichia coli was transformed with these plasmids, cultured to permit cell growth and fusion protein synthesis, then temp.-shifted to cause protein E prodn. and cell lysis. The bacterial ***ghosts*** prepd. were incubated with a hepatitis B core antigen-biotin conjugate to prep. an immunogen.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IN ***Lubitz, Werner*** ; Szostak, Michael P.
AB . . . to permit cell growth and fusion protein synthesis, then temp.-shifted to cause protein E prodn. and cell lysis. The bacterial ***ghosts*** prepd. were incubated with a hepatitis B core antigen-biotin conjugate to prep. an immunogen.
ST antigen membrane anchor fusion Escherichia; lytic protein bacterial ***ghost*** immunogen; vaccine recombinant bacteria ***ghost***
IT Vaccines
(bacterial ***ghosts*** contg. membrane-assocd. recombinant antigens for, prepn. of)
IT Avidins
RL: PREP (Preparation)
(fusion products with membrane-anchoring domains, recombinant manuf. in Escherichia coli of, prepn. of cell ***ghosts*** for vaccines of, bacteriophage lytic functions in)

IT Antigens
RL: PREP (Preparation)
(fusion proteins with membrane-anchoring domains of, Gram-neg. bacterial ***ghosts*** contg., prepn. of, bacteriophage lytic functions in, vaccines in relation to)
IT Escherichia coli
(***ghosts*** of, antigens anchored to membranes of, bacteriophage lytic functions in, vaccines in relation to)
IT Virus, bacterial
(lytic functions of, in prepn. Gram-neg. bacterial ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)
IT Proteins, biological studies
RL: PREP (Preparation)
(lytic, of bacteriophage, in prepn. Gram-neg. bacterial ***ghosts*** contg. of antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)
IT Mammal
(vaccines for, antigens for, bacterial ***ghosts*** contg. membrane-assocd. recombinant antigens as)
IT Proteins, specific or class
RL: PREP (Preparation)
(E, of bacteriophage .phi.X174, in prepn. of Gram-neg. bacterial ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)
IT Proteins, specific or class
RL: PREP (Preparation)
(L, of bacteriophage MS2, in prepn. of Gram-neg. bacterial ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)
IT Virus, bacterial
(MS2, protein L of, in prepn. Gram-neg. bacterial ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)
IT Sialoglycoproteins
RL: PREP (Preparation)
(gp120env, fusion products, with bacteriophage proteins E or L, membrane anchoring in Escherichia coli of, prepn. of ***ghosts*** for vaccines in relation to)
IT Glycoproteins, specific or class
RL: PREP (Preparation)
(gp41env, fusion products, with bacteriophage proteins E or L, membrane anchoring in Escherichia coli of, prepn. of ***ghosts*** for vaccines in relation to)
IT Antigens
RL: BIOL (Biological study)
(hepatitis B core, conjugate with biotin, complex with Escherichia coli ***ghosts*** contg. membrane-bound streptavidin, as immunogen)
IT Virus, bacterial
(phi X174, protein E of, in prepn. Gram-neg. bacterial ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)
IT 9013-20-1D, Streptavidin, fusion products with membrane-anchoring protein 9031-11-2D, .beta.-Galactosidase, fusion products with phage E or L proteins
RL: BIOL (Biological study)
(membrane-bound, recombinant manuf. in Escherichia coli of, prepn. of

cell ***ghosts*** for vaccines of, bacteriophage lytic functions in)

L2 ANSWER 54 OF 54 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1989:132089 CAPLUS <<LOGINID::20090617>>
DN 110:132089
OREF 110:21735a,21738a
TI Biochemical characterization of .vphi.X174 protein E-mediated lysis of Escherichia coli
AU Witte, Angela; ***Lubitz, Werner***
CS Inst. Microbiol. Genet., Univ. Vienna, Vienna, A-1090, Austria
SO European Journal of Biochemistry (1989), 180(2), 393-8
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB Energetic and permeability properties of E. coli cells were detd. prior to and during lysis caused by expression of the cloned gene E of phage .phi.X174. Before the onset of cell lysis, the transmembrane gradients for K+, Na+, or Mg2+ ions, the level of ATP and the membrane potential were unaffected. All these parameters changed simultaneously at the time of lysis onset, as monitored by measurements of culture turbidity as well as by detg. the various specifications over a period of 1 min. During cell lysis, chromosomal DNA was fragmented, whereas plasmid DNA ws liberated in its intact, supercoiled form. Cytoplasmic constituents were released almost entirely, as indicated by the activity of .beta.-galactosidase in the supernatant fraction of protein E-lysed cells. Periplasmic enzymes were only found in limited amts. in the cell supernatant, and most remained assocd. with the cell ***ghosts*** . Such ***ghosts*** exhibited no gross cell damage or morphol. alterations when compared with intact E. coli by light microscopy. All parameters investigated indicated that protein E-mediated lysis of E. coli is caused by the formation of a transmembrane tunnel structure through the envelope complex of the bacterium.
AU Witte, Angela; ***Lubitz, Werner***
AB . . . cells. Periplasmic enzymes were only found in limited amts. in the cell supernatant, and most remained assocd. with the cell ***ghosts*** . Such ***ghosts*** exhibited no gross cell damage or morphol. alterations when compared with intact E. coli by light microscopy. All parameters investigated. . .

=> s (bacterial ghost?)
L5 400 (BACTERIAL GHOST?)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 131 DUP REM L5 (269 DUPLICATES REMOVED)

=> s l6 and (biotin or avid or streptavidin or antibod? or receptor)
L7 23 L6 AND (BIOTIN OR AVID OR STREPTAVIDIN OR ANTIBOD? OR RECEPTOR)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 23 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2009:252748 BIOSIS <<LOGINID::20090617>>

DN PREV200900252748
TI Mice orally vaccinated with Edwardsiella tarda ghosts are significantly protected against infection.
AU Wang, Xuepeng; Lu, Chengping [Reprint Author]
CS Nanjing Agr Univ, Key Lab Anim Dis Diagnost and Immunol, Minist Agr, Nanjing 210095, Peoples R China
xpwang@sdau.edu.cn; lucp@njau.edu.cn
SO Vaccine, (MAR 4 2009) Vol. 27, No. 10, pp. 1571-1578.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 8 Apr 2009
Last Updated on STN: 8 Apr 2009
AB ***Bacterial*** ***ghosts*** may be generated by the controlled expression of the phiX174 lysis gene E in Gram-negative bacteria and they are intriguing vaccine candidates since ghosts retain functional antigenic cellular determinants often lost during traditional inactivation procedures. The Edwardsiella tarda ghost (ETG) vaccine was prepared using this technology and tested in vaccination trials. Control groups included mice immunized with formalin-killed E tarda (FKC) or mice treated with phosphate-buffered saline (PBS), respectively. The results showed that serum IgA and IgG ***antibody*** titers were significantly higher in the ETG-vaccinated group compared to the other groups. In addition, CD8+ T cell counts in peripheral blood were elevated in the ETG groups. Most important, ETG-immunized mice were significantly protected against E. tarda challenge (86.7% survival) compared to 73.3 and 33.3% survival in the FKC-immunized and PBS-treated control, respectively, Suggesting that an ETG oral vaccine could confer protection against infection in a mouse model of disease. (C) 2009 Elsevier Ltd. All rights reserved.
AB ***Bacterial*** ***ghosts*** may be generated by the controlled expression of the phiX174 lysis gene E in Gram-negative bacteria and they are intriguing. . . formalin-killed E tarda (FKC) or mice treated with phosphate-buffered saline (PBS), respectively. The results showed that serum IgA and IgG ***antibody*** titers were significantly higher in the ETG-vaccinated group compared to the other groups. In addition, CD8+ T cell counts in. . .

L7 ANSWER 2 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2009:123003 BIOSIS <<LOGINID::20090617>>
DN PREV200900123003
TI ***Bacterial*** ***ghosts*** as a delivery system for zona pellucida-2 fertility control vaccines for brushtail possums (Trichosurus vulpecula).
AU Walcher, Petra; Cui, Xianlan; Arrow, Jane A.; Scobie, Susie; Molinia, Frank C.; Cowan, Phil E.; Lubitz, Werner; Duckworth, Janine A. [Reprint Author]
CS Landcare Res, POB 40, Lincoln 7640, New Zealand
duckworthj@landcareresearch.co.nz
SO Vaccine, (DEC 9 2008) Vol. 26, No. 52, pp. 6832-6838.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 11 Feb 2009
Last Updated on STN: 11 Feb 2009
AB The introduced brushtail possum is a serious pest in New Zealand and there is much interest in the development of an immunocontraceptive vaccine for population control. Immunisation of female possums against recombinant

possum zona pellucida protein-2 (ZP2) is known to reduce embryo production by 72-75% but successful development of fertility control will depend on a delivery system that is effective ***Bacterial*** ***ghost*** vaccine technology is a promising system to formulate a non-living vaccine for for field use. bait or aerosol delivery. The N-terminal (amino acid residues 41-316, ZP2N) and C-terminal (amino acid residues 308-636, ZP2C) regions of possum ZP2 were fused to maltose-binding protein and expressed in the periplasmic space of Escherichia coli NM522 ***bacterial*** ***ghosts*** . Female possums (n = 20 per treatment group) were immunised with 20 mg of either plain ghosts, ZP2N ghosts, or ZP2C ghosts in phosphate-buffered saline applied to the nostrils and eyes (nasal/conjunctival mucosa) at weeks 0, 2 and 4. Effects of immunisation on fertility were assessed following superovulation and artificial insemination. Both constructs evoked humoral (***antibody***) and cell-mediated immune responses in possums and significantly fewer eggs were fertilised in females immunised against ZP2C ghosts. Results in this study indicate that ***bacterial*** ***ghosts*** containing possum ZP antigens can reduce possum fertility when delivered by mucosal immunisation and offer a promising delivery system for fertility control of wild possum populations. (C) 2008 Elsevier Ltd. All rights reserved.

TI ***Bacterial*** ***ghosts*** as a delivery system for zona pellucida-2 fertility control vaccines for brushtail possums (Trichosurus vulpecula).

AB. . . reduce embryo production by 72-75% but successful development of fertility control will depend on a delivery system that is effective ***Bacterial*** ***ghost*** vaccine technology is a promising system to formulate a non-living vaccine for for field use. bait or aerosol delivery. The. . . ZP2C) regions of possum ZP2 were fused to maltose-binding protein and expressed in the periplasmic space of Escherichia coli NM522 ***bacterial*** ***ghosts*** . Female possums (n = 20 per treatment group) were immunised with 20 mg of either plain ghosts, ZP2N ghosts, or. . . 0, 2 and 4. Effects of immunisation on fertility were assessed following superovulation and artificial insemination. Both constructs evoked humoral (***antibody***) and cell-mediated immune responses in possums and significantly fewer eggs were fertilised in females immunised against ZP2C ghosts. Results in this study indicate that ***bacterial*** ***ghosts*** containing possum ZP antigens can reduce possum fertility when delivered by mucosal immunisation and offer a promising delivery system for. . .

IT Methods & Equipment
bacterial ***ghost*** : drug delivery device

IT Miscellaneous Descriptors
immune response

L7 ANSWER 3 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2008:340257 BIOSIS <<LOGINID::20090617>>

DN PREV200800340256

TI Generation of Aeromonas hydrophila ghosts and their evaluation as oral vaccine candidates in Carassius auratus gibelio.

AU Chu, Weihua; Zhuang, Xiyi; Lu, Chengping [Reprint Author]

CS Nanjing Agr Univ, Coll Vet Med, Nanjing 210095, Peoples R China
lucp@njau.edu.cn

SO Weishengwu Xuebao, (FEB 2008) Vol. 48, No. 2, pp. 202-206.
CODEN: WSHPA8. ISSN: 0001-6209.

DT Article

LA Chinese

ED Entered STN: 5 Jun 2008
Last Updated on STN: 18 Jun 2008

AB The ***bacterial*** ***ghost*** (BG) system is a novel vaccine delivery system endowed with intrinsic adjuvant properties.
Bacterial ***ghosts*** are nonliving Gram-negative bacterial cell envelopes devoid of cytoplasmic contents while maintaining their cellular morphology and native surface antigenic structures. They are produced by PhiX174 protein E-mediated lysis of Gram-negative bacteria, and can induce humoral and cellular immune response, including mucosal immune responses. Plasmid pElysis consisting E gene was transformed into AhJ-1. Through shifting the culture temperature from 28 degrees C to 421 degrees C, A. hydrophila J-1 (pElysis) was induced to lyse and the OD600 value of culture media was measured every 15 minutes during the induction. The lysed bacteria were observed by scanning electron microscopy (SEM). The A. hydrophila ghosts (AHG) used as oral vaccine were also investigated. The OD600 value of A. hydrophila J-1(pElysis) began to decline after 30min of induction, and after 75min of induction, the OD600 value decline speed become slowly. The efficiency of ghost induction in non-lyophilized A.hydrophila was 99.99%, 16 hours post induced, no live bacteria can be detected in culture. Scanning electron microscopy observation proved that most lysed bacteria were emptied. Fish vaccination experiments shows that the ***antibody*** evoked highest degree after 5 weeks by oral administration of ***bacterial*** ***ghost*** vaccine and the agglutination ***antibody*** titer reached 2 7 and continued two weeks, while the agglutination ***antibody*** titer of formalin killed vaccine only reached 2 6 and only maintained one week. After challenged with the parent strain J-1, the survival rate of ***bacterial*** ***ghost*** vaccinated fish was higher than the control group and formalin killed vaccine group, the relative percent survival (RPS) was 78.95% (16/20), but the RPS of formalin killed vaccine group was 57.9% (12/20). This suggests that the ***bacterial*** ***ghost*** vaccine has higher potential to induce protective adaptive immunity than normal vaccine.

AB The ***bacterial*** ***ghost*** (BG) system is a novel vaccine delivery system endowed with intrinsic adjuvant properties.
Bacterial ***ghosts*** are nonliving Gram-negative bacterial cell envelopes devoid of cytoplasmic contents while maintaining their cellular morphology and native surface antigenic structures.. . . detected in culture. Scanning electron microscopy observation proved that most lysed bacteria were emptied. Fish vaccination experiments shows that the ***antibody*** evoked highest degree after 5 weeks by oral administration of ***bacterial*** ***ghost*** vaccine and the agglutination ***antibody*** titer reached 2 7 and continued two weeks, while the agglutination ***antibody*** titer of formalin killed vaccine only reached 2 6 and only maintained one week. After challenged with the parent strain J-1, the survival rate of ***bacterial*** ***ghost*** vaccinated fish was higher than the control group and formalin killed vaccine group, the relative percent survival (RPS) was 78.95% (16/20), but the RPS of formalin killed vaccine group was 57.9% (12/20). This suggests that the ***bacterial*** ***ghost*** vaccine has higher potential to induce protective adaptive immunity than normal vaccine.

IT . . .
hydrophila infection: bacterial disease, prevention and control

IT Chemicals & Biochemicals
formalin; E gene; PhiX174 protein E; pElysis plasmid; agglutination

antibody ; Aeromonas hydrophild ghost vaccine: immunologic-drug,
immunostimulant-drug, oral administration, production, vaccine

L7 ANSWER 4 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:458038 BIOSIS <<LOGINID::20090617>>
DN PREV200300458038
TI Pasteurella multocida- and Pasteurella haemolytica-ghosts: New vaccine candidates.
AU Marchart, J.; Dropmann, G.; Lechleitner, S.; Schlapp, T.; Wanner, G.; Szostak, M. P. [Reprint Author]; Lubitz, W.
CS BIRD-C GmbH, Schonborngasse 12/12, A-1080, Vienna, Austria
szostak@bird-c.com
SO Vaccine, (8 September 2003) Vol. 21, No. 25-26, pp. 3988-3997. print.
ISSN: 0264-410X (ISSN print).
DT Article
LA English
ED Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003
AB Pasteurella multocida is an important animal pathogen. ***Bacterial*** ***ghosts*** produced by the expression of phage PhiX174 lysis gene E are empty cells devoid of cytoplasmic and genomic material. Lysis of P. multocida 7A and P. haemolytica A1 carrying Pasteurella-specific lysis vectors (pSR2 and pSON2) occurred 140 min after induction of gene E expression induced by temperature upshift. The E-mediated cell lysis and killing activity was the same in both Pasteurella species and no viable cells could be detected after lysis of P. multocida and P. haemolytica. Pasteurella ghosts were used for immunization of rabbits and mice. Rabbits immunized subcutaneously with either P. multocida- or P. haemolytica-ghosts developed ***antibodies*** reacting with the immunizating strain, as well as with other Pasteurella strains. The number of proteins in whole cell protein extracts recognized by the sera constantly increased during the observation period of 51 days. In addition, dose-dependent protection against homologous challenge was observed in mice immunized with P. multocida-ghosts. Animals which received 1.15 X 108 ghosts and a challenge dose of up to 60 cfu (LD90), showed 100% protection. According to these results, we suggest ghosts of P. multocida and P. haemolytica as new vaccine candidates.
AB Pasteurella multocida is an important animal pathogen. ***Bacterial*** ***ghosts*** produced by the expression of phage PhiX174 lysis gene E are empty cells devoid of cytoplasmic and genomic material. Lysis. . . ghosts were used for immunization of rabbits and mice. Rabbits immunized subcutaneously with either P. multocida- or P. haemolytica-ghosts developed ***antibodies*** reacting with the immunizating strain, as well as with other Pasteurella strains. The number of proteins in whole cell protein. . .
IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis); Infection
IT Chemicals & Biochemicals
antibodies ; lysis vectors; phage PhiX174

L7 ANSWER 5 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:439696 BIOSIS <<LOGINID::20090617>>
DN PREV200300439696
TI Construction of recombinant S-layer proteins (rSbsA) and their expression in ***bacterial*** ***ghosts*** : A delivery system for the

nontypeable Haemophilus influenzae antigen Omp26.
AU Riedmann, Eva M. [Reprint Author]; Kyd, Jennelle M.; Smith, Adam M.; Gomez-Gallego, Sara; Jalava, Katri; Cripps, Allan W.; Lubitz, Werner
CS Institute of Microbiology and Genetics, University of Vienna, Vienna Biocentre, 1090, Vienna, Austria
eva.riedmann@univie.ac.at
SO FEMS Immunology and Medical Microbiology, (15 July 2003) Vol. 37, No. 2-3, pp. 185-192. print.
ISSN: 0928-8244 (ISSN print).
DT Article
LA English
ED Entered STN: 24 Sep 2003
Last Updated on STN: 24 Sep 2003
AB This study has investigated the feasibility of a combination of recombinant surface layer (S-layer) proteins and empty bacterial cell envelopes (ghosts) to deliver candidate antigens for a vaccine against nontypeable Haemophilus influenzae (NTHi) infections. The S-layer gene sbsA from Bacillus stearothermophilus PV72 was used for the construction of fusion proteins. Fusion of maltose binding protein (MBP) to the N-terminus of SbsA allowed expression of the S-layer in the periplasm of Escherichia coli. The outer membrane protein (Omp) 26 of NTHi was inserted into the N-terminal and C-terminal regions of SbsA. The presence of the fused antigen Omp26 was demonstrated by Western blot experiments using anti-Omp26 antisera. Electron microscopy showed that the recombinant SbsA maintained the ability to self-assemble into sheet-like and cylindrical structures. Recombinant E. coli cell envelopes (ghosts) were produced by the expression of SbsA/Omp26 fusion proteins prior to gene E-mediated lysis. Intraperitoneal immunization with these recombinant ***bacterial*** ***ghosts*** induced an Omp26-specific ***antibody*** response in BALB/c mice. These results demonstrate that the NTHi antigen, Omp26, was expressed in the S-layer self-assembly product and this construct was immunogenic for Omp26 when administered to mice in bacterial cell envelopes.
TI Construction of recombinant S-layer proteins (rSbsA) and their expression in ***bacterial*** ***ghosts*** : A delivery system for the nontypeable Haemophilus influenzae antigen Omp26.
AB. . . (ghosts) were produced by the expression of SbsA/Omp26 fusion proteins prior to gene E-mediated lysis. Intraperitoneal immunization with these recombinant ***bacterial*** ***ghosts*** induced an Omp26-specific ***antibody*** response in BALB/c mice. These results demonstrate that the NTHi antigen, Omp26, was expressed in the S-layer self-assembly product and. . .
IT . . .
carboxyl-terminal, recombinant, surface layer protein; SbsA-Omp26 fusion protein: immunologic-drug, immunostimulant-drug; nontypeable Haemophilus influenzae infection vaccine: immunologic-drug, immunostimulant-drug, pharmacodynamics; recombinant S-layer protein-***bacterial*** ***ghost*** combination [rSbsA- ***bacterial*** ***ghost*** combination]: immunologic-drug, immunostimulant-drug, construction, expression

L7 ANSWER 6 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:597049 BIOSIS <<LOGINID::20090617>>
DN PREV200200597049
TI Induction of heterologous protection in rabbits by Vibrio cholerae ghosts (VCG) expressing toxin co-regulated pili.
AU Eko, F. O. [Reprint author]; Schukovskaya, T. N.; Lotzmanova, E. Y.;

Firstova, V. V.; Emalyanova, N. V.; Klueva, S. N.; Kravtzov, A. L.; Livanova, L. F.; Kutyrev, V. V.; Igietseme, J. U.; Lubitz, W.

CS Morehouse School of Medicine, Atlanta, GA, USA

SO Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 199. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology.
ISSN: 1060-2011.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002

AB An effective Vibrio cholerae vaccine would reduce the morbidity and mortality caused by this pathogen. Parenterally administered cholera vaccines have been disappointing. Current live attenuated and inactivated vaccines are not ideal. The recent emergence of the 0139 serogroup of V. cholerae with epidemic potential poses a new problem in cholera vaccine development. Immunity to the pre-existing 01 strains offers no protection against infection by V. cholerae 0139, indicating a need for vaccines to combat the latter. Toxin-coregulated pili (TCP) induce protection against both the 01 and 0139 serogroups in infant mice. Although only weakly immunogenic in man, the inclusion of these pili in vaccine formulations may enhance protective efficacy by promoting mucosal immunity. ***Bacterial*** ***ghosts*** , produced by expression of cloned lysis gene E, possess strong adjuvant properties and are immunogenic. In this study, ghosts were prepared from strains of V. cholerae 01 or 0139 and evaluated as vaccines in the removable intestinal tie adult rabbit (RITARD) model. Rabbits were intragastrically immunized with graded doses of TCP-positive or TCP-negative VCGs. Sera were assayed for vibriocidal ***antibodies*** . Rabbits were challenged intraduodenally, 30 days after the first immunization and monitored for diarrhea, colonization and death. Regardless of the TCP status of the VCG preparations used for immunization, all animals produced ***antibodies*** to LPS as demonstrated by serum vibriocidal titer rises against indicator strains. The induction of cross protection was evidenced by the ability of serum from immunized rabbits to mediate complement-dependent killing of homologous and heterologous strains. Protective immunity against challenge appeared to be dose dependent and was associated with marked inhibition of colonization. These results indicate that VCG expressing TCP may represent a novel approach to cholera vaccine development.

AB. . . weakly immunogenic in man, the inclusion of these pili in vaccine formulations may enhance protective efficacy by promoting mucosal immunity. ***Bacterial*** ***ghosts*** , produced by expression of cloned lysis gene E, possess strong adjuvant properties and are immunogenic. In this study, ghosts were. . . rabbit (RITARD) model. Rabbits were intragastrically immunized with graded doses of TCP-positive or TCP-negative VCGs. Sera were assayed for vibriocidal ***antibodies*** . Rabbits were challenged intraduodenally, 30 days after the first immunization and monitored for diarrhea, colonization and death. Regardless of the TCP status of the VCG preparations used for immunization, all animals produced ***antibodies*** to LPS as demonstrated by serum vibriocidal titer rises against indicator strains. The induction of cross protection was evidenced by. . .

IT . . .

Infection; Pharmacology
IT Parts, Structures, & Systems of Organisms
pili
IT Diseases
cholera: bacterial disease
Cholera (MeSH)
IT Chemicals & Biochemicals
antibodies ; antigens; cholera vaccines: applications, development; complement; microbial vaccines: applications, development; proteins

L7 ANSWER 7 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:223205 BIOSIS <<LOGINID::20090617>>
DN PREV200200223205
TI Immunogenicity of a novel recombinant subunit candidate vaccine against Chlamydia trachomatis.
AU Eko, F. O. [Reprint author]; Lubitz, W.; Igietseme, J. U. [Reprint author]
CS Morehouse School of Medicine, Atlanta, GA, USA
SO Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 341. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society of Microbiology.
ISSN: 1060-2011.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002
AB An efficacious vaccine is needed to control the morbidity and huge healthcare cost associated with genital infection by C. trachomatis. In accordance with the new paradigm for vaccine design, an efficacious anti-chlamydial vaccine should elicit a genital mucosal Th1 response. Despite considerable efforts, the development of reliable chlamydial vaccines using conventional strategies has proven to be elusive. Genetic inactivation of select bacteria to produce ghosts by the controlled expression of cloned bacteriophage lysis gene E offers a promising new approach in non-living vaccine technology. These ***bacterial*** ***ghosts*** are attractive for use as non-living vaccines; they possess
strong adjuvant properties, maintain the structural and functional integrity of the intact organism, and are excellent vehicles for delivery of foreign or heterologous proteins and other antigens of vaccine relevance to the primary antigen-presenting cells. To design a candidate vaccine against Chlamydia based on the ghost technology, the gene encoding the major outer membrane protein (MOMP), ompl, of C. trachomatis serovar D was expressed in the epitheliotropic bacterium, Vibrio cholerae, as a lacZ'-L' or F'-L' fusion protein targeted to the cell membrane. Following production of recombinant V. cholerae ghosts (rVCG), the integrity and native conformational assembly of MOMP were assessed by immunoblotting analysis and indirect immunofluorescence. Results revealed that MOMP-specific monoclonal ***antibodies*** recognized the expressed rMOMP in immunoblots of ghost lysates. rMOMP was also detected by indirect immunofluorescence staining. Intranasal and intramuscular immunization of naive mice with ghosts expressing rMOMP induced a strong Th1 response in the genital mucosa. The ability of this vaccine regimen to protect susceptible animals from chlamydial infection will establish it as a

potentially efficacious vaccine capable of protecting against human infections. The rVCG system offers a unique opportunity for designing recombinant subunit vaccines capable of simultaneously presenting multiple membrane proteins to the immune system.

AB. . . by the controlled expression of cloned bacteriophage lysis gene E offers a promising new approach in non-living vaccine technology. These ***bacterial*** ***ghosts*** are attractive for use as non-living vaccines; they possess strong adjuvant properties, maintain the structural and functional integrity of the. . . integrity and native conformational assembly of MOMP were assessed by immunoblotting analysis and indirect immunofluorescence. Results revealed that MOMP-specific monoclonal ***antibodies*** recognized the expressed rMOMP in immunoblots of ghost lysates. rMOMP was also detected by indirect immunofluorescence staining. Intranasal and intramuscular. . .

L7 ANSWER 8 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2000:467776 BIOSIS <<LOGINID::20090617>>
DN PREV200000467776
TI Improved protection against lung colonization by Actinobacillus pleuropneumoniae ghosts: Characterization of a genetically inactivated vaccine.
AU Huter, Veronika; Hensel, Andreas; Brand, Edith; Lubitz, Werner [Reprint author]
CS Section for Microbiology and Biotechnology, Biocenter, Institute of Microbiology and Genetics, University of Vienna, A-1030, Vienna, Austria
SO Journal of Biotechnology, (29 September, 2000) Vol. 83, No. 1-2, pp. 161-172. print.
CODEN: JBITD4. ISSN: 0168-1656.
DT Article
LA English
ED Entered STN: 1 Nov 2000
Last Updated on STN: 10 Jan 2002
AB Pigs immunized with Actinobacillus pleuropneumoniae ghosts or a formalin-inactivated bacterin were found to be protected against clinical disease in both vaccination groups, whereas colonization of the lungs with A. pleuropneumoniae was only prevented in ghost-vaccinated pigs. ***Bacterial*** ***ghosts*** are empty cell envelopes created by the expression of a cloned bacteriophage lysis gene and, unlike formalin-inactivated bacteria, suffer no denaturing steps during their production. This quality may lead to a superior presentation of surface antigens to the immune system. Analysis by SDS-PAGE and immunoblotting of the two vaccine preparations revealed different contents of antigenic proteins. In order to better understand the immunogenic properties of A. pleuropneumoniae ghosts and formalin-inactivated bacteria, we compared the serum ***antibody*** response induced in both treatment groups. Immune sera were tested on whole cell antigen or purified virulence factors including outer membrane protein preparations (OMPs), outer membrane lipoprotein OmlA1, transferrin binding proteins (TfbA1, TfbA7 and TfbB) and Apx toxins (ApxI, II and III). SDS-PAGE and immunoblots revealed no specific ***antibody*** response against the single virulence factors tested in any vaccinated animal. The two vaccination groups showed different recognition patterns of whole cell antigen and OMP-enriched preparations. A 100 kDa protein was recognized significantly stronger by ghost-vaccinated pigs than convalescent pigs. This unique ***antibody*** population induced by ghosts could play a determining role in the prevention of lung colonization. The same 100 kDa antigen was

recognized by ghost-sera in homologous as well as heterologous serotype A. pleuropneumoniae protein preparations. Indications for a crossprotective potential in the ghost vaccine were supported by studies on rabbit hyperimmune sera.

AB. . . clinical disease in both vaccination groups, whereas colonization of the lungs with A. pleuropneumoniae was only prevented in ghost-vaccinated pigs. ***Bacterial*** ***ghosts*** are empty cell envelopes created by the expression of a cloned bacteriophage lysis gene and, unlike formalin-inactivated bacteria, suffer no. . . proteins. In order to better understand the immunogenic properties of A. pleuropneumoniae ghosts and formalin-inactivated bacteria, we compared the serum ***antibody*** response induced in both treatment groups. Immune sera were tested on whole cell antigen or purified virulence factors including outer. . . transferrin binding proteins (TfbA1, TfbA7 and TfbB) and Apx toxins (ApxI, II and III). SDS-PAGE and immunoblots revealed no specific ***antibody*** response against the single virulence factors tested in any vaccinated animal. The two vaccination groups showed different recognition patterns of. . . antigen and OMP-enriched preparations. A 100 kDa protein was recognized significantly stronger by ghost-vaccinated pigs than convalescent pigs. This unique ***antibody*** population induced by ghosts could play a determining role in the prevention of lung colonization. The same 100 kDa antigen. . .

IT . . .
(Chemical Coordination and Homeostasis); Infection; Veterinary Medicine (Medical Sciences); Pharmacology; Respiratory System (Respiration)

IT Parts, Structures, & Systems of Organisms
bacterial ***ghosts*** , uses; lungs: respiratory system, bacterial colonization, protection

IT Chemicals & Biochemicals
antigens; bacterial proteins; bacterial vaccines: development, preparation; genetically inactivated. . .

L7 ANSWER 9 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2000:467771 BIOSIS <<LOGINID::20090617>>
DN PREV200000467771
TI Characterization and immunogenicity of Vibrio cholerae ghosts expressing toxin-coregulated pili.
AU Eko, F. O. [Reprint author]; Mayr, U. B.; Attridge, S. R.; Lubitz, W.
CS Department of Microbiology and Immunology, Morehouse School of Medicine, 720 Westview Drive, S.W., Atlanta, GA, 30310, USA
SO Journal of Biotechnology, (29 September, 2000) Vol. 83, No. 1-2, pp. 115-123. print.
CODEN: JBITD4. ISSN: 0168-1656.
DT Article
LA English
ED Entered STN: 1 Nov 2000
Last Updated on STN: 10 Jan 2002

AB ***Bacterial*** ***ghosts*** are attractive for use as non-living vaccines and as carriers of heterologous antigens of vaccine relevance. Ghosts were prepared from Vibrio cholerae strains of O1 or O139 serogroup after growth under culture conditions, which favor or repress the production of toxin-coregulated pili (TCP). Immunoblotting confirmed the TCP status of these V. cholerae ghosts (VCG), which retained the cellular morphology and envelope sub-component profile of viable bacteria. Rabbits were immunized with VCGs prepared from O139 bacteria with TCP-positive or TCP-negative phenotypes and the resulting sera assayed for ***antibodies*** to lipopolysaccharide (LPS) and to TCP. Regardless of

the TCP status of the VCG preparations used for immunization, all animals produced ***antibodies*** to LPS as demonstrated in bactericidal assays. These ***antibodies*** were probably responsible for the capacity of the antisera to confer passive immunity to challenge with the homologous O139 strain in the infant mouse cholera model (IMCM). Only following immunization with TCP-positive VCG, however, were ***antibodies*** to TCP generated, as judged by the potential of antisera to mediate protection against a challenge strain of heterologous serogroup.

AB ***Bacterial*** ***ghosts*** are attractive for use as non-living vaccines and as carriers of heterologous antigens of vaccine relevance. Ghosts were prepared from. . . Rabbits were immunized with VCGs prepared from O139 bacteria with TCP-positive or TCP-negative phenotypes and the resulting sera assayed for ***antibodies*** to lipopolysaccharide (LPS) and to TCP. Regardless of the TCP status of the VCG preparations used for immunization, all animals produced ***antibodies*** to LPS as demonstrated in bactericidal assays. These ***antibodies*** were probably responsible for the capacity of the antisera to confer passive immunity to challenge with the homologous O139 strain in the infant mouse cholera model (IMCM). Only following immunization with TCP-positive VCG, however, were ***antibodies*** to TCP generated, as judged by the potential of antisera to mediate protection against a challenge strain of heterologous serogroup.

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology

IT Parts, Structures, & Systems of Organisms
bacterial ***ghosts*** , characterization, immunogenicity;
pili

IT Diseases
cholera: bacterial disease, prevention
Cholera (MeSH)

IT Chemicals & Biochemicals
antibodies ; bacterial antigens; bacterial proteins; bacterial
toxins; bacterial vaccines: development, preparation; lipopolysaccharides

L7 ANSWER 10 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2000:355995 BIOSIS <<LOGINID::20090617>>

DN PREV200000355995

TI Intramuscular immunization with genetically inactivated (ghosts) Actinobacillus pleuropneumoniae serotype 9 protects pigs against homologous aerosol challenge and prevents carrier state.

AU Hensel, Andreas [Reprint author]; Huter, Veronika; Katinger, Astrid; Raza, Peter; Strnistschie, Christine; Roesler, Uwe; Brand, Edith; Lubitz, Werner

CS Veterinary Faculty, Institute of Animal Hygiene and Veterinary Public Health, University of Leipzig, D-04103, Leipzig, Germany

SO Vaccine, (1 July, 2000) Vol. 18, No. 26, pp. 2945-2955. print. CODEN: VACCDE. ISSN: 0264-410X.

DT Article

LA English

ED Entered STN: 16 Aug 2000
Last Updated on STN: 8 Jan 2002

AB ***Bacterial*** ***ghosts*** are empty cell envelopes achieved by

the expression of a cloned bacteriophage lysis gene and, unlike classical bacterins, suffer no denaturing steps during their production. These properties may lead to a superior presentation of surface antigens to the immune system. Currently available porcine Actinobacillus pleuropneumoniae vaccines afford only minimal protection by decreasing mortality but not morbidity. Pigs which survive infection can still be carriers of the pathogen, so a herd once infected remains infected. Carrier pigs harbour A. pleuropneumoniae in their nasal cavities, in their tonsils, or within lung lesions. A dose-defined nose-only aerosol infection model for pigs was used to study the immunogenic and protective potential of systemic immunization with ghosts made from A. pleuropneumoniae serotype 9 reference strain CVI 13261 against an homologous aerogenous challenge. Pigs were vaccinated twice intramuscularly with a dose of 5 X 109 CFU ghosts (GVPs) or formalin-inactivated A. pleuropneumoniae bacterins (BVPs). After 2 weeks vaccinated pigs and non-vaccinated placebo controls (PCs) were challenged with a dose of 109 CFU by aerosol. The protective efficacy of immunization was evaluated by clinical, bacteriological, serological and post-mortem examinations. Bronchoalveolar lavage in pigs was performed during the experiment to obtain lavage samples (BALF) for assessment of local ***antibodies*** . Isotype-specific ***antibody*** responses in serum and BALF were determined by ELISAs based on whole-cell antigen. Immunization with ghosts did not cause clinical side-effects. After aerosol challenge PCs developed fever and pleuropneumonia. GVPs or BVPs were found to be fully protected against clinical disease or lung lesions in both vaccination groups, whereas colonization of the respiratory tract with A. pleuropneumoniae was only prevented in GVPs. Specific immunoglobins against A. pleuropneumoniae were not detectable in BALF after immunization. A significant systemic increase of IgM, IgA, IgG(Fc'), or IgG(H + L) ***antibodies*** reactive with A. pleuropneumoniae was measured in GVPs and BVPs when compared to the non-exposed controls. BVPs reached higher titers of IgG(Fc') and IgG(H + L) than GVPs. However, prevention of carrier state in GVPs coincided with a significant increase of serum IgA when compared to BVPs. These results suggest that immunization with ghosts, that bias ***antibody*** populations specific to non-denaturated surface antigens, may be more efficacious in protecting pigs against colonization and infection than bacterins.

AB ***Bacterial*** ***ghosts*** are empty cell envelopes achieved by the expression of a cloned bacteriophage lysis gene and, unlike classical bacterins, suffer no. . . post-mortem examinations. Bronchoalveolar lavage in pigs was performed during the experiment to obtain lavage samples (BALF) for assessment of local ***antibodies*** . Isotype-specific ***antibody*** responses in serum and BALF were determined by ELISAs based on whole-cell antigen. Immunization with ghosts did not cause clinical. . . pleuropneumoniae were not detectable in BALF after immunization. A significant systemic increase of IgM, IgA, IgG(Fc'), or IgG(H + L) ***antibodies*** reactive with A. pleuropneumoniae was measured in GVPs and BVPs when compared to the non-exposed controls. BVPs reached higher titers. . . with a significant increase of serum IgA when compared to BVPs. These results suggest that immunization with ghosts, that bias ***antibody*** populations specific to non-denaturated surface antigens, may be more efficacious in protecting pigs against colonization and infection than bacterins.

L7 ANSWER 11 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN
AN 2000:42619 BIOSIS <<LOGINID::20090617>>
DN PREV200000042619
TI Bacterial cell envelopes (ghosts) but not S-layers activate human endothelial cells (HUVECs) through sCD14 and LBP mechanism.
AU Furst-Ladani, Shayesteh [Reprint author]; Redl, Heinz; Haslberger, Alexander; Lubitz, Werner; Messner, Paul; Sleytr, Uwe B.; Schlag, Gunther
CS Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Donaueschingenstrasse 13, 1200, Vienna, Austria
SO Vaccine, (Oct., 1999) Vol. 18, No. 5-6, pp. 440-448. print.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 26 Jan 2000
Last Updated on STN: 31 Dec 2001
AB Bacterial cell-envelopes (called ghosts) and surface layers (S-layers) are discussed to be used as vaccines and/or adjuvants, consequently it is necessary to find out which immunomodulatory mediators are induced in human cells. The present work focuses on the effects of ghosts (Escherichia coli O26:B6), S-layers (Bacillus stearothermophilus) in comparison with LPS and antibiotic-inactivated whole bacteria (E. coli O26:B6) on human umbilical vein endothelial cells (HUVEC) with regard to the release of interleukin 6 (IL-6) and the expression of surface E-selectin and the role of lipopolysaccharide binding protein (LBP), soluble CD14 (sCD14) and serum for this activation. Endothelial cells responded to ghosts, whole bacteria and LPS with IL-6 release up to 15000 pg/ml and surface E-selectin expression, while in contrast the response to S-layers with IL-6 release up to 500 pg/ml was very weak. Compared to LPS, 10-100-fold higher concentrations of ***bacterial*** ***ghosts*** and whole bacteria were required to induce the cytokine synthesis and E-selectin expression. IL-6 release and E-selectin expression of HUVECs were reduced in the absence of serum and equivalent to unstimulated samples. We have also studied the role of CD14 and LBP for the activation of endothelial cells using antiCD14 and antiLBP ***antibodies*** (Ab). AntiCD14 and antiLBP Ab both inhibited IL-6 release and E-selectin expression in a dose dependent manner after stimulation with ghosts, whole bacteria and LPS but had no effect on S-layers stimulated cells. AntiCD14 Ab inhibited more effectively than antiLBP Ab. These findings suggest that ***bacterial*** ***ghosts*** but not S-layers activate HUVECs through sCD14 and LBP dependent mechanisms.
AB. . . response to S-layers with IL-6 release up to 500 pg/ml was very weak. Compared to LPS, 10-100-fold higher concentrations of ***bacterial*** ***ghosts*** and whole bacteria were required to induce the cytokine synthesis and E-selectin expression. IL-6 release and E-selectin expression of HUVECs. . . We have also studied the role of CD14 and LBP for the activation of endothelial cells using antiCD14 and antiLBP ***antibodies*** (Ab). AntiCD14 and antiLBP Ab both inhibited IL-6 release and E-selectin expression in a dose dependent manner after stimulation with. . . but had no effect on S-layers stimulated cells. AntiCD14 Ab inhibited more effectively than antiLBP Ab. These findings suggest that ***bacterial*** ***ghosts*** but not S-layers activate HUVECs through sCD14 and LBP dependent mechanisms.

L7 ANSWER 12 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2000:9740 BIOSIS <<LOGINID::20090617>>

DN PREV200000009740
TI ***Bacterial*** ***ghosts*** as drug carrier and targeting vehicles.
AU Huter, Veronika [Reprint author]; Szostak, Michael P.; Gampfer, Joerg; Prethaler, Saskia; Wanner, Gerhard; Gabor, Franz; Lubitz, Werner
CS Institute of Microbiology and Genetics, University of Vienna, Dr. Bohrgasse 9, A-1030, Vienna, Austria
SO Journal of Controlled Release, (Aug. 27, 1999) Vol. 61, No. 1-2, pp. 51-63. print.
CODEN: JCREEC. ISSN: 0168-3659.
DT Article
LA English
ED Entered STN: 23 Dec 1999
Last Updated on STN: 31 Dec 2001
AB A novel system for the packaging of drugs as well as vaccines is presented. ***Bacterial*** ***ghosts*** are intact, non-denatured bacterial envelopes that are created by lysis of bacteria through the expression of cloned phage PhiX174 gene E. Inhibition of induced E-mediated lysis by MgSO4, harvesting of cells by centrifugation, and resuspension in low-ionic-strength buffers leads to rapid, violent lysis and results in empty bacterial envelopes with large (approximately 1 mum in diameter) openings. The construction of plasmid pAV1, which encodes a ***streptavidin*** fusion protein with an N-terminal membrane anchor sequence, allows the loading of the inner side of the cytoplasmic membrane with ***streptavidin*** . The functionality and efficacy of binding of even large biotinylated compounds in such ***streptavidin*** ghosts (SA-ghosts) was assessed using the enzyme alkaline phosphatase. The successful binding of biotinylated fluorescent dextran, as well as fluorescent DNA complexed with biotinylated polylysine, w as demonstrated microscopically. The display by ***bacterial*** ***ghosts*** of morphological and antigenic surface structures of their living counterparts permits their attachment to target tissues such as the mucosal surfaces of the gastrointestinal and respiratory tract, and their uptake by phagocytes and M cells. In consequence, SA-ghosts are proposed as drug carriers for site-specific drug delivery.
TI ***Bacterial*** ***ghosts*** as drug carrier and targeting vehicles.
AB A novel system for the packaging of drugs as well as vaccines is presented. ***Bacterial*** ***ghosts*** are intact, non-denatured bacterial envelopes that are created by lysis of bacteria through the expression of cloned phage PhiX174 gene. . . in empty bacterial envelopes with large (approximately 1 mum in diameter) openings. The construction of plasmid pAV1, which encodes a ***streptavidin*** fusion protein with an N-terminal membrane anchor sequence, allows the loading of the inner side of the cytoplasmic membrane with ***streptavidin*** . The functionality and efficacy of binding of even large biotinylated compounds in such ***streptavidin*** ghosts (SA-ghosts) was assessed using the enzyme alkaline phosphatase. The successful binding of biotinylated fluorescent dextran, as well as fluorescent DNA complexed with biotinylated polylysine, w as demonstrated microscopically. The display by ***bacterial*** ***ghosts*** of morphological and antigenic surface structures of their living counterparts permits their attachment to target tissues such as the mucosal. . .
IT . . .
Pharmacology
IT Parts, Structures, & Systems of Organisms

membrane
IT Chemicals & Biochemicals
biotinylated fluorescent dextran; fluorescent DNA; plasmid pAV1; ***streptavidin***
IT Miscellaneous Descriptors
streptavidin -ghost: drug carrier, drug targeting vehicle
RN 9013-20-1 (***streptavidin***)

L7 ANSWER 13 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1999:468971 BIOSIS <<LOGINID::20090617>>
DN PREV199900468971
TI Pigs aerogenously immunized with genetically inactivated (ghosts) or irradiated Actinobacillus pleuropneumoniae are protected against a homologous aerosol challenge despite differing in pulmonary cellular and ***antibody*** responses.
AU Katinger, Astrid; Lubitz, Werner; Szostak, Michael P.; Stadler, Maria; Klein, Reinhard; Indra, Alexander; Huter, Veronika; Hensel, Andreas [Reprint author]
CS Institute of Animal Hygiene and Veterinary Public Health, University of Leipzig, Semmelweisstr. 4, D-04103, Leipzig, Germany
SO Journal of Biotechnology, (Aug. 20, 1999) Vol. 73, No. 2-3, pp. 251-260. print.
CODEN: JBITD4. ISSN: 0168-1656.
DT Article
LA English
ED Entered STN: 9 Nov 1999
Last Updated on STN: 9 Nov 1999
AB Aerosol immunization is a safe way to induce complete protection against pleuropneumonia in pigs caused by the lung pathogenic bacterium Actinobacillus pleuropneumoniae. In order to determine the local immune responses of vaccines in concomitant with protection, lung lining fluid before and 3 weeks after immunization from pigs immunized three times with aerosols of either genetically inactivated ghosts which represent whole cell envelope preparations, or irradiated bacteria were examined following an homologous aerosol challenge. Specific ***antibody*** isotypes in the bronchoalveolar lavage were assayed by whole cell ELISAs. Total and relative numbers of cells including lymphocyte subsets were determined. In both vaccinated groups a net influx of plasma cells and lymphocytes, as well as a significant increase of specific IgG occurred. Concurrently, the CD4+/CD8+ ratio was found to increase after aerosol immunization. The lymphocyte subsets of IgG+ and IgA+ cells were found significantly higher in the group immunized with irradiated bacteria when compared to pigs immunized with ***bacterial*** ***ghosts*** . The latter group showed a significant increase of IgA, IgM, and a net influx of lymphoid blasts and granulocytes in the bronchoalveolar lining fluid. Although differences between the local immune responses of both immunized groups occurred, a significant increase of specific IgG and a net influx of plasma cells and lymphocytes were found to be associated with complete protection against a homologous aerosol challenge infection.
TI. . . genetically inactivated (ghosts) or irradiated Actinobacillus pleuropneumoniae are protected against a homologous aerosol challenge despite differing in pulmonary cellular and ***antibody*** responses.
AB. . . genetically inactivated ghosts which represent whole cell envelope preparations, or irradiated bacteria were examined following an homologous aerosol challenge. Specific ***antibody*** isotypes in the bronchoalveolar lavage were assayed by whole cell ELISAs. Total and

relative numbers of cells including lymphocyte subsets. . . and IgA+ cells were found significantly higher in the group immunized with irradiated bacteria when compared to pigs immunized with ***bacterial*** ***ghosts*** . The latter group showed a significant increase of IgA, IgM, and a net influx of lymphoid blasts and granulocytes in. . .

IT Methods & Equipment
aerosol immunization: immunization method, vaccine delivery method; genetically inactivated ghost aerosol immunization: immunization method

IT Miscellaneous Descriptors
antibody response; immune response; vaccine development

L7 ANSWER 14 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 1998:362918 BIOSIS <<LOGINID::20090617>>

DN PREV199800362918

TI Bacterial cell envelopes (ghosts) and LPS but not bacterial S-layers induce synthesis of immune-mediators in mouse macrophages involving CD14.

AU Haslberger, A. G. [Reprint author]; Mader, H. J.; Schmalnauer, M.; Kohl, G.; Szostak, M. P.; Messner, P.; Sleytr, U. B.; Wanner, G.; Fuerst-Ladani, S.; Lubitz, W.

CS Inst. Microbiology Genetics, Biocenter, Univ. Vienna, Dr Bohrgrasse 9, A-1030 Vienna, Austria

SO Journal of Endotoxin Research, (Dec., 1997) Vol. 4, No. 6, pp. 431-441. print.
ISSN: 0968-0519.

DT Article

LA English

ED Entered STN: 27 Aug 1998
Last Updated on STN: 27 Aug 1998

AB The synthesis of inflammatory mediators in human macrophages/monocytes seen after stimulation with lipopolysaccharide (LPS) involves the binding of CD14 to LPS complexed to lipopolysaccharide binding protein (LBP). The binding mechanisms of different LPS domains to LBP and CD14, as well as the interaction of the entire bacterial cell wall and its components with CD14 and LBP, are poorly understood. We, therefore, studied the effects of antimouse CD14 ***antibodies*** on the synthesis of TNFalpha and PGE2 in RAW 264.7 mouse macrophages stimulated by bacterial cell envelopes (ghosts) of Escherichia coli 026:B6 and Salmonella typhimurium C5, LPS, lipid A, and crystalline bacterial cell surface layer (S-layer) preparations. Ghosts and S-layers, with distinct activities on the immune-system, are presently under investigation for their use as vaccines. Whereas LPS and E. coli ghosts exhibited a strong endotoxic activity in the Limulus amoebocyte lysate assay, the endotoxic activity of S-layer preparations was several orders of magnitude lower. LPS, ghosts, and bacterial S-layers all induced TNFalpha and PGE2 synthesis as well as the accumulation of TNFalpha mRNA. Pre-incubation with anti-mouse CD14 ***antibodies*** resulted in a dose-dependent inhibition of TNFalpha and PGE2 synthesis after stimulation by LPS, lipid A (30-50%) and ghosts (40-70%). The bacterial S-layer-induced mediator synthesis remained unchanged following the addition of anti-mouse CD14 ***antibodies*** . Reproducible differences could be observed for the inhibition of TNFalpha induced by LPS of different species by anti-CD14. Adding fetal calf serum (FCS) strongly enhanced the release of cell mediators stimulated by low doses of LPS and ***bacterial*** ***ghosts*** . These effects of the FCS may be due to the presence of LBP in the FCS. The results show that CD14 is highly relevant for the activation of mouse macrophages by

bacterial cells, LPS, and lipid A. Specially defined bacterial cell wall constituents such as bacterial S-layers might act through other activation pathways.

AB. . . cell wall and its components with CD14 and LBP, are poorly understood. We, therefore, studied the effects of antimouse CD14 ***antibodies*** on the synthesis of TNFalpha and PGE2 in RAW 264.7 mouse macrophages stimulated by bacterial cell envelopes (ghosts) of Escherichia. . . bacterial S-layers all induced TNFalpha and PGE2 synthesis as well as the accumulation of TNFalpha mRNA. Pre-incubation with anti-mouse CD14 ***antibodies*** resulted in a dose-dependent inhibition of TNFalpha and PGE2 synthesis after stimulation by LPS, lipid A (30-50%) and ghosts (40-70%). The bacterial S-layer-induced mediator synthesis remained unchanged following the addition of anti-mouse CD14 ***antibodies*** . Reproducible differences could be observed for the inhibition of TNFalpha induced by LPS of different species by anti-CD14. Adding fetal calf serum (FCS) strongly enhanced the release of cell mediators stimulated by low doses of LPS and ***bacterial*** ***ghosts*** . These effects of the FCS may be due to the presence of LBP in the FCS. The results show that. . .

IT . . .

IT Parts, Structures, & Systems of Organisms
macrophages: blood and lymphatics, immune system

IT Chemicals & Biochemicals
anti-mouse CD14 monoclonal ***antibodies*** ; bacterial cell envelopes [ghosts]; lipid A; lipopolysaccharide binding protein; mRNA [messenger RNA]; prostaglandin E2: synthesis; tumor necrosis factor-alpha: synthesis; CD14;. . .

L7 ANSWER 15 OF 23 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 1997:180858 BIOSIS <<LOGINID::20090617>>

DN PREV199799472571

TI Endotoxicity does not limit the use of ***bacterial*** ***ghosts*** as candidate vaccines.

AU Mader, Horst J.; Szostak, Michael P.; Hensel, Andreas; Lubitz, Werner; Haslberger, Alexander G. [Reprint author]

CS Inst. Microbiol. Genetics, Univ. Vienna, Biocenter Dr. Bohrgasse 9, Vienna, A-1030, Austria

SO Vaccine, (1997) Vol. 15, No. 2, pp. 195-202.
CODEN: VACCDE. ISSN: 0264-410X.

DT Article

LA English

ED Entered STN: 24 Apr 1997
Last Updated on STN: 24 Apr 1997

AB Gram-negative ***bacterial*** ***ghosts*** produced by controlled expression of the plasmid-encoded lysis gene E offers a promising approach in non-living vaccine technology. Bacterial cell wall complex and hence the antigenic determinants of the living cells are not affected by denaturation due to cell killing. However, the endotoxin content of the Gram-negative cell wall has been discussed as a potential problem for this kind of whole cell or envelope vaccines. Here we show that ***bacterial*** ***ghosts*** prepared from Escherichia coli O26:B6 and Salmonella typhimurium C5 induce dose-dependent ***antibody*** responses against bacterial cells or their corresponding lipopolysaccharides (LPS) in doses 25 ng kg-1 when administered intravenously to rabbits in a standard immunization protocol. No differences between the immune responses of the rabbits were observed when

comparing equivalent doses of ***bacterial*** ***ghosts*** and antibiotic-treated whole cells. The results indicate that the ***bacterial*** ***ghosts*** exhibit all the antigenic properties of the living cells. No significant fever responses in rabbits have been recorded in doses of lt 250 ng kg-1 E. coli O26:B6 ghosts and up to doses of 250 ng kg-1 S. typhimurium C5 ghosts when applying test methods recommended by the US pharmacopoeia. These findings correlate with cell culture experiments where doses 100 ng ml-1 of ***bacterial*** ***ghosts*** were needed for the release of tumour necrosis factor alpha (TNF-alpha) and prostaglandin E-2 (PGE-2) from RAW mouse macrophage cultures. Free LPS of Salmonella abortus equi commonly used as a LPS-standard, however, stimulated TNF-alpha and PGE-2 synthesis of RAW cells in doses of 1 ng ml-1. The endotoxic activity of our bacterial preparations analysed by a standard limulus amoebocyte lysate and 2-keto-3-deoxyoctonate assay correlated with the capacity to stimulate the release of PGE-2 and TNF-alpha in RAW mouse macrophage cultures and the endotoxic responses in rabbits. It can be concluded that these in vitro systems can be used as easy predictive test systems for preparations of bacterial vaccines, particularly for ***bacterial*** ***ghosts*** .

TI Endotoxicity does not limit the use of ***bacterial*** ***ghosts*** as candidate vaccines.

AB Gram-negative ***bacterial*** ***ghosts*** produced by controlled expression of the plasmid-encoded lysis gene E offers a promising approach in non-living vaccine technology. Bacterial cell. . . has been discussed as a potential problem for this kind of whole cell or envelope vaccines. Here we show that ***bacterial*** ***ghosts*** prepared from Escherichia coli O26:B6 and Salmonella typhimurium C5 induce dose-dependent ***antibody*** responses against bacterial cells or their corresponding lipopolysaccharides (LPS) in doses 25 ng kg-1 when administered intravenously to rabbits in. . . a standard immunization protocol. No differences between the immune responses of the rabbits were observed when comparing equivalent doses of ***bacterial*** ***ghosts*** and antibiotic-treated whole cells. The results indicate that the ***bacterial*** ***ghosts*** exhibit all the antigenic properties of the living cells. No significant fever responses in rabbits have been recorded in doses. . . test methods recommended by the US pharmacopoeia. These findings correlate with cell culture experiments where doses 100 ng ml-1 of ***bacterial*** ***ghosts*** were needed for the release of tumour necrosis factor alpha (TNF-alpha) and prostaglandin E-2 (PGE-2) from RAW mouse macrophage cultures.. . . that these in vitro systems can be used as easy predictive test systems for preparations of bacterial vaccines, particularly for ***bacterial*** ***ghosts*** .

IT Miscellaneous Descriptors
ANTIGENICITY; ***BACTERIAL*** ***GHOSTS*** ; C5; DOSE-DEPENDENT ***ANTIBODY*** RESPONSE; ENDOTOXICITY; ENDOTOXIN; IMMUNE SYSTEM; LIPOPOLYSACCHARIDES; MACROPHAGE; O26:B6; PROSTAGLANDIN E-2; RELEASE; TNF-ALPHA; TOXICOLOGY; TUMOR NECROSIS FACTOR-ALPHA

L7 ANSWER 16 OF 23 CABA COPYRIGHT 2009 CABI on STN

AN 2008:83068 CABA <<LOGINID::20090617>>

DN 20063203692

TI Advances in vaccine development against enterohemorrhagic Escherichia coli O157:H7

AU Liu YanQing; Mao XuHu; Zou QuanMing; Liu, Y. Q.; Mao, X. H.; Zou, Q. M.

CS Clinical Microbiology and Immunology, The Third Medical University of PLA, Chongqing 400038, China. mxh95xy@mail.tmmu.com.cn
SO Chinese Journal of Zoonoses, (2006) Vol. 22, No. 10, pp. 998-1000. 23 ref.
Publisher: Editorial Committee of Chinese Journal of Zoonoses, Health and Anti-epidemic Station of Fujian Province. Fuzhou
ISSN: 1002-2694
URL: http://www.zgrsghbzz.periodicals.net.cn
CY China
DT Journal
LA Chinese
ED Entered STN: 5 May 2008
Last Updated on STN: 5 May 2008
AB Vaccine related protective antigens of enterohemorrhagic Escherichia coli O157:H7 include adhesion antigens (e.g. intimin, translocated intimin ***receptor*** and type III secretion system related protein EspA) and toxic antigens. Polysaccharide vaccine, subunit vaccine, transgenic plant vaccine and ***bacterial*** ***ghost*** vaccine have been developed. Some vaccines have already been put into clinical trials.
AB Vaccine related protective antigens of enterohemorrhagic Escherichia coli O157:H7 include adhesion antigens (e.g. intimin, translocated intimin ***receptor*** and type III secretion system related protein EspA) and toxic antigens. Polysaccharide vaccine, subunit vaccine, transgenic plant vaccine and ***bacterial*** ***ghost*** vaccine have been developed. Some vaccines have already been put into clinical trials.

L7 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:1171779 CAPLUS <<LOGINID::20090617>>
DN 147:467781
TI Her-2/neu multi-peptide cancer vaccine
IN Zielinski, Christoph; Schreiner, Otto; Pehamberger, Hubert; Breiteneder, Heimo; Wiedermann, Ursula
PA Bio Life Science Forschungs- und Entwicklungsges.m.b.H., Austria
SO Eur. Pat. Appl., 26pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1844788	A1	20071017	EP 2006-7834	20060413
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	AU 2007237491	A1	20071025	AU 2007-237491	20070411
	CA 2649013	A1	20071025	CA 2007-2649013	20070411
	WO 2007118660	A2	20071025	WO 2007-EP3226	20070411
	WO 2007118660	A3	20071213		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,				

GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 2004218 A2 20081224 EP 2007-724167 20070411

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR

PRAI EP 2006-7834 A 20060413

WO 2007-EP3226 W 20070411

AB A multi-peptide multiepitope vaccine against cancers assocd. with HER-2/neu oncogene overexpression is disclosed. The vaccine comprises a specific combination of peptides presenting different amino acids sequences that are present in the extracellular domain of HER-2/neu protein. The inventors demonstrate that the above vaccine is effective in preventing neu-expressing tumors and that the effect could be increased by co-administration of interleukin-12. Also, the vaccine could be administered as a mucosal vaccine without losing its high immunogenicity, which would be an attractive vaccine for tumors located at mucosal surfaces.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT ***Antibodies*** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgA; her-2/neu multi-peptide cancer vaccine)

IT ***Antibodies*** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG1; her-2/neu multi-peptide cancer vaccine)

IT ***Antibodies*** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IgG2a; her-2/neu multi-peptide cancer vaccine)

IT Drug delivery systems
(***bacterial*** ***ghosts*** , vaccine carriers; her-2/neu multi-peptide cancer vaccine)

IT Interleukin 2
Interleukin 4
neu (***receptor***)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(her-2/neu multi-peptide cancer vaccine)

L7 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:120755 CAPLUS <<LOGINID::20090617>>

DN 142:225686

TI Sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions

IN Lubitz, Werner

PA Austria

SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005011713	A1	20050210	WO 2004-EP8790	20040805

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE	10335796	A1	20050303	DE 2003-10335796	20030805
AU	2004260620	A1	20050210	AU 2004-260620	20040805
AU	2004260620	B2	20080124		
CA	2534612	A1	20050210	CA 2004-2534612	20040805
EP	1656149	A1	20060517	EP 2004-763831	20040805
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
NZ	545232	A	20081224	NZ 2004-545232	20040805
US	20060286126	A1	20061221	US 2006-567426	20060516
PRAI DE	2003-10335796	A	20030805		
WO	2004-EP8790	W	20040805		

AB The invention relates to a method for producing sealed ***bacterial*** ***ghosts*** using the specific interaction between partners of a binding pair. The ghosts can be loaded with therapeutically useful substances and used as carriers. The inventive sealed ghosts can be used in medicine, agriculture, and biotechnol. Ghosts are formed by inducing expression of the E gene, which causes membrane lysis. The ghosts are then derivatized with a member of a binding pair, e.g. ***biotin*** , or a ***streptavidin*** -binding peptide. Biotinylation may be via an enzymic biotinylation site incorporated into the E gene product. The derivatized ghosts are then mixed with lipid vesicles present the other member of the binding pair, e.g. ***streptavidin*** . The interaction results in the binding of the lipid vesicles to the ghosts. Sealed ghosts can be captured using the ligand immobilized on a suitable carrier.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions

AB The invention relates to a method for producing sealed ***bacterial*** ***ghosts*** using the specific interaction between partners of a binding pair. The ghosts can be loaded with therapeutically useful substances and. . . the E gene, which causes membrane lysis. The ghosts are then derivatized with a member of a binding pair, e.g. ***biotin*** , or a ***streptavidin*** -binding peptide. Biotinylation may be via an enzymic biotinylation site incorporated into the E gene product. The derivatized ghosts are then mixed with lipid vesicles present the other member of the binding pair, e.g. ***streptavidin*** . The interaction results in the binding of the lipid vesicles to the ghosts. Sealed ghosts can be captured using the. . .

ST bacteria membrane ghost sealing lipid vesicle affinity interaction; membrane ***biotin*** vesicle ***streptavidin*** bacteria ghost sealing

IT Gene, microbial
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(E; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Drug delivery systems
(***bacterial*** ***ghosts*** as; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity

ligand interactions)
IT Transformation, genetic
(***bacterial*** ***ghosts*** for delivery of nucleic acids in; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Agrochemicals
Drugs
Dyes
Organelle
(***bacterial*** ***ghosts*** for delivery of; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Nucleic acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***bacterial*** ***ghosts*** for delivery of; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Protein motifs
(biotinylation, lysis proteins contg.; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Protoplast and Spheroplast
(cell ghost; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Virion structure
(envelope, sealing of membrane ghosts with; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT ***Antibodies*** and Immunoglobulins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(fragments, in affinity binding of membrane vesicles to ***bacterial*** ***ghosts*** ; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Agglutinins and Lectins
Antibodies and Immunoglobulins
Avidins
Carbohydrates, biological studies
Haptens
Receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in affinity binding of membrane vesicles to ***bacterial*** ***ghosts*** ; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Eubacteria
(membrane ghosts; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Proteins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(membrane, incorporation into ***bacterial*** ***ghosts*** of; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)
IT Immobilization, molecular or cellular
(of ***bacterial*** ***ghosts*** ; sealing of ***bacterial***

ghosts for drug delivery using membrane vesicles and affinity ligand interactions)

IT Gram-negative bacteria
(prepn. of membrane ghosts from; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Agriculture and Agricultural chemistry
Biotechnology
Medicine
(sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Liposomes
(sealing of membrane ghosts with; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT Lipids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(vesicles, sealing of membrane ghosts with; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT 58-85-5D, ***Biotin*** , analogs, conjugates with proteins 9013-20-1, ***Streptavidin***
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in affinity binding of membrane vesicles to ***bacterial*** ***ghosts*** ; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT 842177-75-7 842177-76-8 842177-77-9 842177-78-0 842177-79-1 842177-80-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

IT 842138-49-2
RL: PRP (Properties)
(unclaimed sequence; sealing of ***bacterial*** ***ghosts*** for drug delivery using membrane vesicles and affinity ligand interactions)

L7 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:66560 CAPLUS <<LOGINID::20090617>>
DN 143:1800
TI DNA-loaded ***bacterial*** ***ghosts*** efficiently mediate reporter gene transfer and expression in macrophages
AU Paukner, Susanne; Kudela, Pavol; Kohl, Gudrun; Schlapp, Tobias; Friedrichs, Sonja; Lubitz, Werner
CS Institute of Microbiology and Genetics, Vienna University Biocenter, Vienna, A-1030, Austria
SO Molecular Therapy (2005), 11(2), 215-223
CODEN: MTOHCK; ISSN: 1525-0016
PB Elsevier
DT Journal
LA English
AB There is a demand for efficient and safe DNA delivery vehicles mediating gene transfer and expression. We present ***bacterial***

ghosts as a novel platform technol. for DNA delivery and targeting
of macrophages. ***Bacterial*** ***ghosts*** are cell envelopes of gram-neg. bacteria that are devoid of the cytoplasmic content. Escherichia coli ghosts were loaded with plasmid DNA and linear double-stranded DNA. Confocal laser scanning microscopy and flow cytometry confirmed that the DNA localized to the inner lumen of ***bacterial*** ***ghosts*** and was not assocd. with the outer surface of the bacteria. Up to .apprx.6000 plasmids could be loaded per single ghost and the amt. of loaded DNA correlated with the DNA concn. used for loading. E. coli ghosts loaded with plasmids encoding the enhanced green fluorescent protein (EGFP) targeted efficiently murine macrophages (RAW264.7) and mediated effective gene transfer. The EGFP was expressed by more than 60% of the macrophages as measured by flow cytometry detecting the green fluorescence and immunocytochem. staining with ***antibodies*** specific for EGFP.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI DNA-loaded ***bacterial*** ***ghosts*** efficiently mediate reporter gene transfer and expression in macrophages

AB There is a demand for efficient and safe DNA delivery vehicles mediating gene transfer and expression. We present ***bacterial*** ***ghosts*** as a novel platform technol. for DNA delivery and targeting
of macrophages. ***Bacterial*** ***ghosts*** are cell envelopes of gram-neg. bacteria that are devoid of the cytoplasmic content. Escherichia coli ghosts were loaded with plasmid. . . linear double-stranded DNA. Confocal laser scanning microscopy and flow cytometry confirmed that the DNA localized to the inner lumen of ***bacterial*** ***ghosts*** and was not assocd. with the outer surface of the bacteria. Up to .apprx.6000 plasmids could be loaded per single. . . by more than 60% of the macrophages as measured by flow cytometry detecting the green fluorescence and immunocytochem. staining with ***antibodies*** specific for EGFP.

IT Cell envelope
(***bacterial*** ***ghosts*** ; plasmid and linear dsDNA-loaded ***bacterial*** ***ghosts*** efficiently mediate reporter gene transfer and expression in mouse macrophages)

IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(double-stranded, linear; plasmid and linear dsDNA-loaded ***bacterial*** ***ghosts*** efficiently mediate reporter gene transfer and expression in mouse macrophages)

IT Escherichia coli
Macrophage
Plasmid vectors
Transformation, genetic
(plasmid and linear dsDNA-loaded ***bacterial*** ***ghosts*** efficiently mediate reporter gene transfer and expression in mouse macrophages)

L7 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:377951 CAPLUS <<LOGINID::20090617>>
DN 136:364204
TI Marsupial contraceptive vaccine targeting the zona pellucida
IN Mate, Karen; McCartney, Carmen; Duckworth, Janine; Bradley, Mark
PA Marsupial Crc Limited, Australia

SO Pat. Specif. (Aust.), 45 pp.
CODEN: ALXXAP
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	AU 735248	B2	20010705	AU 1998-78554	19980729
	AU 9878554	A	19990211		
PRAI	AU 1997-8354	A	19970731		

AB The present invention relates to isolated marsupial zona pellucida (ZP2 and ZP3) polypeptides and to polynucleotides encoding these polypeptides. The present invention also relates to a contraceptive vaccine compn. contg. either the polypeptides or polynucleotides for use in a marsupial female and to a method of inhibiting conception in marsupials. Chimeric polypeptides are also claimed comprising a polypeptide of the invention and a second polypeptide, including keyhole limpet hemocyanin and tetanus toxoid. ***Antibodies*** to the polypeptides are also claimed.
AB . . . are also claimed comprising a polypeptide of the invention and a second polypeptide, including keyhole limpet hemocyanin and tetanus toxoid. ***Antibodies*** to the polypeptides are also claimed.
IT Vaccines
(live, ***bacterial*** ***ghost*** ; marsupial contraceptive vaccine contg. zona pellucida polypeptides and polynucleotides)

L7 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:623585 CAPLUS <<LOGINID::20090617>>
DN 133:227782
TI ***Bacterial*** ***ghosts*** as carrier and targeting vehicles
IN Huter, Veronika; Lubitz, Werner
PA Austria
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19909770	A1	20000907	DE 1999-19909770	19990305
	CA 2370714	A1	20000914	CA 2000-2370714	20000303
	WO 2000053163	A1	20000914	WO 2000-EP1906	20000303
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1158966	A1	20011205	EP 2000-912549	20000303
	EP 1158966	B1	20030611		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002538198	T	20021112	JP 2000-603652	20000303
	AT 242630	T	20030615	AT 2000-912549	20000303
	NZ 514408	A	20040130	NZ 2000-514408	20000303
	AU 778166	B2	20041118	AU 2000-34272	20000303

PRAI DE 1999-19909770 A 19990305
WO 2000-EP1906 W 20000303

AB Empty bacterial envelopes (ghosts), produced by controlled heterologous expression of a gene which effects a partial lysis of the cell membrane, are useful as carriers and targeting vehicles for active substances and markers. They may be administered via the natural infection pathways for pathogenic bacteria and are delivered specifically to the target tissues of the bacteria with high efficiency. Being empty, they can be loaded with active substances to a high degree. Agents which can be packaged in the ghosts include drugs, polypeptides, nucleic acids, agrochems., dyes, inks, and cosmetics; these may be immobilized by binding to specific receptors or binding sites incorporated into or anchored to the ghosts. Thus, Escherichia coli NM522 cells were transformed simultaneously with plasmid pML1 (contg. phage .phi.X174 gene E encoding a transmembrane protein which induces leakage of the cell contents) and plasmid pAV1 (contg. the 54 5'-terminal codons of gene E fused in-frame to a coding sequence for the protease factor Xa recognition sequence and to 160 codons of the ***streptavidin*** gene). Expression of the ***streptavidin*** gene was induced with 3 mM IPTG, and expression of lysis protein E was subsequently induced by raising the temp. from 28.degree. to 42.degree.. Centrifugation of the cells and resuspension in distd. water resulted in immediate lysis, producing ghosts to which ***streptavidin*** was anchored. These ghosts strongly bound biotinylated alk. phosphatase, FITC- ***biotin*** , and other biotinylated agents.

TI ***Bacterial*** ***ghosts*** as carrier and targeting vehicles

AB . . . E fused in-frame to a coding sequence for the protease factor Xa recognition sequence and to 160 codons of the ***streptavidin*** gene). Expression of the ***streptavidin*** gene was induced with 3 mM IPTG, and expression of lysis protein E was subsequently induced by raising the temp.. . . 28.degree. to 42.degree.. Centrifugation of the cells and resuspension in distd. water resulted in immediate lysis, producing ghosts to which ***streptavidin*** was anchored. These ghosts strongly bound biotinylated alk. phosphatase, FITC- ***biotin*** , and other biotinylated agents.

ST bacteria ghost drug carrier targeting; ***streptavidin*** bacteria ghost drug carrier

IT Gene, microbial
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(E, of phage .phi.X174, plasmid contg.; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active agent immobilization in matrix of; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Diagnosis
(agents; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Agrochemicals
Anti-infective agents
Antitumor agents
Autoimmune disease
Bacteria (Eubacteria)
Cell membrane
Cytolysis

Drug targeting
Dyes
Gene therapy
Genetic markers
Gram-negative bacteria
Gram-positive bacteria (Firmicutes)
Immobilization, biochemical
Vaccines
(***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Nucleic acids
Reporter gene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Avidins
Polysaccharides, biological studies
Receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Drug delivery systems
(carriers; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fluorescent-labeled; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Coliphage .phi.X174
(gene E protein of, lysis by; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy, polymers; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand-binding; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Aggregation
(matrix formation by; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Enzymes, uses
RL: CAT (Catalyst use); USES (Uses)
(matrix polymn. catalyzed by; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Encapsulation
(microencapsulation; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Plasmids
(***streptavidin*** gene-contg.; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(***streptavidin*** -contg.; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfates; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT 146397-20-8
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(DNA labeled with; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT 25988-63-0, Poly-L-lysine hydrobromide 35013-72-0, ***Biotin*** N-hydroxysuccinimide ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT 9004-54-0, Dextran, biological studies 9013-20-1, ***Streptavidin*** 25104-18-1, Poly-L-lysine 38000-06-5, Poly-L-lysine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***bacterial*** ***ghosts*** as carrier and targeting vehicles)

IT 9001-78-9D, biotinylated 25104-18-1D, Poly-L-lysine, biotinylated 38000-06-5D, Poly-L-lysine, biotinylated 134759-22-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(binding of, to ***streptavidin*** -contg. ***bacterial*** ***ghosts*** ; ***bacterial*** ***ghosts*** as carrier and targeting vehicles)

L7 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1992:1761 CAPLUS <<LOGINID::20090617>>
DN 116:1761
OREF 116:363a,366a
TI Membrane-anchoring of heterologous proteins in recombinant hosts for use as antigens
IN Lubitz, Werner; Szostak, Michael P.
PA Boehringer Mannheim G.m.b.H., Germany
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9113155	A1	19910905	WO 1991-EP308	19910219
	W: AU, FI, HU, JP, SU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	DE 4005874	A1	19911107	DE 1990-4005874	19900224
	AU 9172373	A	19910918	AU 1991-72373	19910219
	EP 516655	A1	19921209	EP 1991-903789	19910219
	EP 516655	B1	19940504		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05503014	T	19930527	JP 1991-503980	19910219
	JP 3238396	B2	20011210		
	AT 105335	T	19940515	AT 1991-903789	19910219
	US 5470573	A	19951128	US 1992-924028	19920930
PRAI	DE 1990-4005874	A	19900224		

EP 1991-903789 A 19910219
WO 1991-EP308 A 19910219

AB Antigenic proteins are prepd. with a Gram-neg. bacteria contg. a gene encoding a lytic protein by expression of a chimeric gene for a fusion protein of a membrane-anchoring domain and the antigen. Plasmid pAV5 encoding a ***streptavidin*** -phage MS2 protein L fusion protein and a plasmid contg. the protein E gene of phage .phi.X174 under control of the temp. sensitive .lambda. repressor-.lambda. promoter/operator system were prepd. Escherichia coli was transformed with these plasmids, cultured to permit cell growth and fusion protein synthesis, then temp.-shifted to cause protein E prodn. and cell lysis. The ***bacterial*** ***ghosts*** prepd. were incubated with a hepatitis B core antigen-***biotin*** conjugate to prep. an immunogen.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB . . . expression of a chimeric gene for a fusion protein of a membrane-anchoring domain and the antigen. Plasmid pAV5 encoding a ***streptavidin*** -phage MS2 protein L fusion protein and a plasmid contg. the protein E gene of phage .phi.X174 under control of the. . . cultured to permit cell growth and fusion protein synthesis, then temp.-shifted to cause protein E prodn. and cell lysis. The ***bacterial*** ***ghosts*** prepd. were incubated with a hepatitis B core antigen- ***biotin*** conjugate to prep. an immunogen.

ST antigen membrane anchor fusion Escherichia; lytic protein ***bacterial*** ***ghost*** immunogen; vaccine recombinant bacteria ghost

IT Vaccines
(***bacterial*** ***ghosts*** contg. membrane-assocd. recombinant antigens for, prepn. of)

IT Antigens
RL: PREP (Preparation)
(fusion proteins with membrane-anchoring domains of, Gram-neg. ***bacterial*** ***ghosts*** contg., prepn. of, bacteriophage lytic functions in, vaccines in relation to)

IT Virus, bacterial
(lytic functions of, in prepn. Gram-neg. ***bacterial*** ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)

IT Proteins, biological studies
RL: PREP (Preparation)
(lytic, of bacteriophage, in prepn. Gram-neg. ***bacterial*** ***ghosts*** contg. of antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)

IT Plasmid and Episome
(pAV3, chimeric gene for ***streptavidin*** -.phi.X174 E and MS2 L protein fusion protein on, expression in Escherichia coli of)

IT Mammal
(vaccines for, antigens for, ***bacterial*** ***ghosts*** contg. membrane-assocd. recombinant antigens as)

IT Proteins, specific or class
RL: PREP (Preparation)
(E, of bacteriophage .phi.X174, in prepn. of Gram-neg. ***bacterial*** ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)

IT Proteins, specific or class
RL: PREP (Preparation)
(L, of bacteriophage MS2, in prepn. of Gram-neg. ***bacterial***

ghosts contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)

IT Virus, bacterial
(MS2, protein L of, in prepn. Gram-neg. ***bacterial*** ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)

IT Antigens
RL: BIOL (Biological study)
(hepatitis B core, conjugate with ***biotin*** , complex with Escherichia coli ghosts contg. membrane-bound ***streptavidin*** , as immunogen)

IT Plasmid and Episome
(pAV1, chimeric gene for ***streptavidin*** -.phi.X174 E protein fusion protein on, expression in Escherichia coli of)

IT Plasmid and Episome
(pAV5, chimeric gene for ***streptavidin*** -MS2 L protein fusion protein on, expression in Escherichia coli of)

IT Virus, bacterial
(phi X174, protein E of, in prepn. Gram-neg. ***bacterial*** ***ghosts*** contg. antigen-membrane-anchoring domain fusion proteins, vaccines in relation to)

IT 137925-62-3, Deoxyribonucleic acid (Escherichia coli clone pMC1403 gene lacZ plus 3'-flanking region fragment) 137925-65-6 137926-10-4, Deoxyribonucleic acid (Streptomyces avidinii clone pAV5 ***streptavidin*** gene plus 5'- and 3'-flanking region fragment)
RL: BIOL (Biological study)
(chimeric gene contg., for fusion protein of membrane-anchoring domain and antigenic determinant, expression in Escherichia coli of, bacteriophage lytic functions in)

IT 9013-20-1D, ***Streptavidin*** , fusion products with membrane-anchoring protein 9031-11-2D, .beta.-Galactosidase, fusion products with phage E or L proteins
RL: BIOL (Biological study)
(membrane-bound, recombinant manuf. in Escherichia coli of, prepn. of cell ghosts for vaccines of, bacteriophage lytic functions in)

L7 ANSWER 23 OF 23 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2005:77370 SCISEARCH <<LOGINID::20090617>>
GA The Genuine Article (R) Number: 883WX
TI Rational design of vaccination strategies to promote antigen entry into the MHC class I-restricted presentation pathway
AU Guzman C A (Reprint)
CS GBF German Res Ctr Biotechnol, Div Microbiol, Vaccine Res Grp, Mascheroder Weg 1, D-38124 Braunschweig, Germany (Reprint)
AU Becker P D
CS GBF German Res Ctr Biotechnol, Div Microbiol, Vaccine Res Grp, D-38124 Braunschweig, Germany
E-mail: cag@gbf.de
CYA Germany
SO TRANSFUSION MEDICINE AND HEMOTHERAPY, (2004) Vol. 31, No. 6, pp. 398-411. ISSN: 1660-3796.
PB KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
DT General Review; Journal
LA English
REC Reference Count: 180
ED Entered STN: 27 Jan 2005

Last Updated on STN: 27 Jan 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cytotoxic CD8+ T lymphocytes (CTLs) constitute one of the main effector mechanisms against tumors and viral infections. CTLs specifically recognize short peptides (8 - 10 residues long) displayed on the surface of 'target' cells, which result from the processing of foreign or abnormal proteins (e. g. virus and tumor proteins) and are bound to major histocompatibility complex (MHC) class I molecules. Virtually all nucleated cells display on their surface fragments of intracellularly produced polypeptides. When there are signs of invasion or transformation, CTLs take control of the situation by destroying these 'labeled' target cells. This is an extremely efficient mechanism. However, the efficient differentiation of naive CD8+ T cells into CTLs is a limiting prerequisite. To achieve this differentiation, dendritic cells (DCs) are critical since only these professional antigen-presenting cells (APCs) can provide not only the peptide presented onto the MHC class I molecules but also the costimulatory signals required for this activation. To this end, DCs take up antigens and degrade them into peptides which are loaded on MHC class I and presented onto the surface to prime specific T lymphocytes. In this review, we summarize the current knowledge on the mechanisms used by professional APCs in the processing and presentation of endogenous and exogenous antigens in the context of MHC class I molecules (i.e. priming and cross-priming). We will also discuss new vaccination strategies that take advantage of these physiological mechanisms in order to improve the elicitation of cytotoxic responses to eliminate intracellular pathogens and tumors.

STP KeyWords Plus (R): COMPLEX CLASS-I; RECOMBINANT LISTERIA-MONOCYTOGENES; CYTOTOXIC T-LYMPHOCYTES; DENDRITIC CELL MATURATION; ***RECEPTOR*** -MEDIATED ENDOCYTOSIS; PROTEIN-CHAPERONED PEPTIDES; EPITOPE PRECURSOR PEPTIDES; EXOGENOUS SOLUBLE-ANTIGEN; ***BACTERIAL*** ***GHOST*** SYSTEM; TOLL-LIKE ***RECEPTOR*** -9